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A NEW ANSWER TO THE QUESTION OF MACULAR SPARING

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According to ordinary field tests, the central visual field is usually spared to a considerable extent when one occipital lobe has been removed or its functions completely destroyed, while the central field is characteristically split vertically when one optic tract is destroyed. If there is actual sparing of the macula in the former case, there seems to be no escape from the conclusion that bilateral representation of the macula exists in the occipital lobes. There is, however, no tenable anatomic evidence in favor of this and in fact much against it¹. Assumption that the supposed sparing is due to instability of fixation fails to solve the enigma because it does not explain why such sparing is not found when one optic tract is destroyed. The theory that I have to offer explains macular sparing after complete destruction of one occipital lobe as only apparent and as due partly to instability of fixation and partly to the establishment of an eccentric fixation point. In addition it accounts for the instability of fixation after lobal destruction and for absence of apparent sparing after interruption of one optic tract. The theory in brief is that apparent sparing results from loss of necessary cortical integration and that this loss may be produced by cortical injury but not by unilateral interruption of the lower visual pathways. The theory rejects bilateral occipital representation of the macula and is based on the following considerations:

Normally during central fixation of a point in space the image of the point is placed nearly on the center of the fovea. This is known from the fact that visual acuity is highest at the fixation point and falls off symmetrically around it. It has been thought that this placement of the image results from an attempt to see the point most distinctly. This, however, is not the case. For it is a well known fact that when foveal vision has become defective in one eye only, or even completely absent, as in the case of a hole in the fovea, the subject will continue to place on the center of the defective fovea the image of any letter he tries to see with this eye alone. In other words, the subject is unable to see any letter he is "looking at" but can see letters near it. It is evident that, at least in the completed organism, central fixation is not controlled by the high visual acuity of the fovea. It therefore must be controlled by integration and correlation of a wide central region with the ocular motor mechanism. Possibly some of the integration takes place in the retina itself, but obviously some of it, the final part, must take place in the cerebral cortex, and an essential part of the corresponding ocular motor coordination must take place here.

If one looks at a circle on a uniform white background and the circle corresponds in size to the macula, one can accurately fixate the center whether or not an actual

1 Hines, M. Recent Contributions to Localization of Vision in the Central Nervous System, Arch Ophth 28 913 (Nov) 1942

point is there. If half the circle is hidden by a large piece of black paper with a straight edge that passes vertically over the center of the circle, one can still precisely fixate the center with the fovea. Evidently, therefore, if the cerebral cortex is intact, the integration and correlation in question can take place when there is no retinal image on one half of the macula. However, since one completes the circle by the imagination, it can be said that there is an imaginary image on one half of the macula. Obviously, when one optic tract is interrupted an analogous condition exists—one half of the visual field is blocked off while the cerebral cortex remains intact. Hence fixation is normal and splitting of the macular field can be found. This would be the case also if corresponding halves of the retinas were destroyed. When, however, one occipital lobe has been destroyed or removed, and the integration in question is thereby abolished, fixation becomes eccentric and apparent sparing is found. It would seem that the new retinal point of fixation would be at about the center of the remaining macula. This would account for apparent sparing of about three fourths of the whole macula. The remainder of the apparent sparing could be accounted for by fixation slippage dependent largely on the altered correlation with the ocular motor mechanism.

Cases have been reported in which a lesion of one occipital lobe has produced hemianopsia with splitting of the macula. In 1 such case the corpus callosum was cut. In Dandy's 3 cases,² in each of which he removed the entire right cerebral hemisphere, it was stated that there was complete hemianopsia.³ While such cases contradict bilateral representation of the macula in the occipital lobes, they may seem also to contradict my theory as thus far presented. To explain these cases the following elaboration of the theory is offered.

Both halves of the visual field of each eye must be represented somewhere or somehow in one or in each of the cerebral hemispheres. For without some sort of visual communication between the two hemispheres, an image presented only in one hemisphere and another image presented only in the other hemisphere could not be compared. Moreover, the communication must be immediate, because the two images can be immediately compared. Simple as are these facts, and obvious as is their implication, they seem to have been generally disregarded. The phenomenon is the same whether the two objects are in the same or in contralateral fields. In some way the two half-fields must be represented as a whole without demarcation between them, for consciously they so appear. Since the two cerebral hemispheres are closely symmetric, it is more than reasonable to believe that a complete visual field is represented in each hemisphere. The site of each representative, which for convenience I shall term the conscious visual area, has not been identified. Possibly it is not in a closely circumscribed area.⁴ It is at this level that the theory of replacement⁵ assumes that each pair of corresponding retinal units is represented by a single unit. Probably, just as the

2 Dandy, W. E. Physiological Studies Following Extirpation of the Right Cerebral Hemisphere in Man, *Bull. Johns Hopkins Hosp.* **53** 31, 1933.

3 It is to be noted, however, that charts of the visual fields are not reproduced and that it is not stated that careful field studies were made. The statement "hemianopsia is of course complete" suggests that completeness was taken for granted and that there may have been apparent sparing in these cases. This question was not discussed by Dandy.

4 The 6 cases reported by A. J. Akelaitis (*Studies on the Corpus Callosum*, *Arch. Neurol. & Psychiat.* **45** 788 [May] 1941) in which the corpus callosum was completely sectioned seem to prove that the visual communication between the two hemispheres is not via the corpus callosum, but via the anterior commissure and therefore suggest that the conscious visual areas are in the temporal lobes.

5 Verhoeff, F. H. A New Theory of Binocular Vision, *Arch. Ophthalm.* **13** 151 (Feb.) 1935.

speech center is situated unilaterally, so the conscious visual area normally employed may be represented unilaterally. In this connection it is of considerable importance that the visual phenomena of squinters who are manifesting anomalous projection can be best explained on the assumption that they are employing one conscious visual area for the right eye and the other for the left eye. Since fixation is largely a voluntary act, it is reasonable to assume that the integration necessary for this act and for conscious visual acuity largely takes place in a conscious visual area, and that in the case of right-handed persons this is usually in the left cerebral hemisphere.

Integration between the two fields would be possible so long as the conscious visual area in use and its motor connections remained intact. As has been pointed out, the integration in question can take place when in one field there is no image from an external source. Therefore splitting of the macular field could be found even after removal of one occipital lobe and complete severance of all connections between the two cerebral hemispheres. If, however, in the conscious visual area used, the function of one macular half was destroyed or seriously impaired, apparent sparing of the macula could be found as I have explained, whether or not the lower visual pathways to this half were intact. Obviously, if the conscious visual area concerned was in the left hemisphere, removal of the left occipital lobe would be more likely to injure directly or indirectly, the left half of this area than would removal of the right lobe. It is noteworthy, therefore, that of the 2 cases reported by Halstead and associates⁶ alleged sparing occurred only in the 1 in which the left lobe was removed. In the case in which the right lobe was removed and no sparing was found, it was definitely stated that the patient was right handed, but in the other case no statement was made as to this question. It may be of importance, also, that the case in which there was no apparent sparing was the one in which it was not certain that all of the striate area had been removed. In a case of hemianopsia, my theory predicts that the less the occipital damage the less the probability of apparent macular sparing. Of course, for real sparing the opposite is true.

Actual sparing without bilateral occipital representation of the macula could occur after complete destruction of one occipital lobe only if visual pathways to the conscious visual area in use could by-pass the injured occipital region. For certain lower animals this may be possible, but for man it would seem not to be so. Yet a case of a boy aged 11 years has been reported⁷ in which one occipital lobe was found at operation to have been completely replaced by a cystic cavity without impairment of visual acuity and without production of hemianopsia or even of important constriction of the visual field. It is to be noted, however, that in this case the lesion began early in life, as the result of birth injury, and that therefore the case is not comparable to cases in which the lesion was acquired much later. Moreover, although discussed, the possibility was not completely excluded that the occipital cortex had simply been pushed aside by the cyst.

Hence if actual sparing of the macula occurred in the case of total lobectomy reported by Halstead and associates,⁶ my explanation is nullified. They took unusual precautions to avoid error. By an electrical method they excluded fixation movements of more than 30 minutes of arc. They also employed a photographic method, but did not state how accurate this was. Presumably it was less

6 Halstead, W. C., Walker, A. E., and Bucy, P. C. Sparing and Non-Sparing of Macular Vision Associated with Occipital Lobectomy in Man, *Arch Ophth* **24** 948 (Nov.) 1940.

7 Jelsma, F., Spurling, R. G., and Freeman, E. Absence of Occipital Lobe of Brain (Porencephaly) with Essentially Normal Vision, *Arch Neurol & Psychiat* **28** 160 (July) 1932.

so than the electrical method, for they did not emphasize it. While it seems certain that they excluded the possibility of ordinary fixation-movements during the field tests, they presented no evidence to exclude the possibility that a gradual slipping of fixation occurred when the patient anticipated that a test object was to be brought from the blind half of the macular field. As a matter of fact, in his original description of his electrical method, Halstead⁸ made the following statement: "The amplitude of eye movements of slower rate than the time constant of the amplifier (approximately one second) will of course be incompletely recorded." It is just such slippage that my theory predicts, and little of it would be required to explain their case on this basis alone. These investigators by refined methods demonstrated sparing of only 1.25 degrees for form and 2.5 degrees for brightness. Other observers by the usual methods repeatedly found sparing of 3 to 5 degrees in the same case. This fact of itself suggests that the extent of apparent sparing varied inversely with refinement of technic and that therefore no actual sparing existed. It is to be noted that in this case the visual acuity, normal in each eye before operation, was reduced in the right eye to 0.8 and in the left eye to 0.8 + 2. This would not be expected if there was actual sparing of the fovea. Apparently also of significance is the fact that in their second case these investigators by means of their refined technic demonstrated splitting, while by usual methods they sometimes found sparing of as much as 2 degrees. This fact accords with the view that there was no actual sparing in either case.

A fixation point eccentric to the extent of 4 degrees of arc would of course be associated with poor visual acuity. Probably an eccentricity of 1.5 degrees in an otherwise normal eye would reduce visual acuity to at least 20/30. How, then, can the fact be explained that in many of the cases under consideration central visual acuity was slightly if at all affected? It is true, as I have indicated, that a person who has acquired defective foveal vision in one eye only will fixate with the defective fovea when the other eye is occluded. In such a case, however, there is ordinarily no reason for him to learn to do otherwise, since the other eye is not defective, and in binocular vision retinal correspondence causes normal bifixation. The circumstances are different when there is hemianopsia with eccentric fixation. Then no doubt the patient soon discovers, consciously or subconsciously, that he must look to one side of an object to see it distinctly and therefore does so when his visual acuity is tested and the best is insisted on. On the other hand, in a visual field test it is not the fixation object but the approaching test object that he is desirous of seeing distinctly. Hence he permits the image of the fixation object to occupy the eccentric macular area or to slip still farther from the real fovea.

There remains to be explained why apparent sparing does not extend above and below the macula. This can be explained on one or all of three reasonable assumptions. The first is that fixation would become less eccentric, that is, approach the normal, when the necessary attention was given to a test object above or below the fixation point. The second is that the subject would consciously or subconsciously discover that he could not make the approaching test object appreciably more distinct by permitting the fixation object to become less distinct. The third assumption is that at a distance from the fovea loss of integration across the margin of the blind field would produce a wider zone of impaired visual perception than it would near the fovea. Thus when a small test object

⁸ Halstead, W. C. A Method for the Quantitative Recording of Eye Movements, *J. Psychol.* 6:177, 1938.

was brought in from the blind field along the horizontal midline, it would be seen sooner than when it was brought in from above or below the fixation point. To elucidate this question further, and to evaluate the relative importance of these assumptions, field tests other than those which have already been used in such cases would need to be employed.

W. Fuchs⁹ has described what he terms a pseudofovea as occurring in certain cases of hemianopsia. By this he meant a retinal area which has a higher visual acuity than the real fovea. While he intimated that he has made similar observations in other cases, he rested his contention on 1 case, to which he devoted a separate lengthy report^{9b}. He stated that there was no sparing of the macula in this case, but here he seems to have begged the question. For all the results he obtained can best be explained on the assumption that there was actual sparing. Moreover, it is impossible to determine the extent of the damage to the occipital lobe in this case or in any of the 3 previous cases he reported^{9a}. He described no case in which one occipital lobe had been completely destroyed and did not discuss the question as to whether the site of the lesion concerns the pseudofovea. For these reasons, his findings, while interesting from a psychologic viewpoint, cannot be regarded as of important significance in connection with the subject of bilateral representation of the macula. The most that can safely be said of them in this connection is that they do not controvert my explanation of apparent sparing, and possibly lend some support to it.

CONCLUSIONS

Apparent sparing of the macula after complete destruction of one occipital lobe is explained by loss of integration between the seeing field and the blind field in the conscious visual cortical area in use. As a result of this loss an eccentric retinal point is employed for fixation, and slipping of fixation easily occurs. The original macular field is actually split through the center but in field tests appears to be more or less spared.

When one optic tract is interrupted, the integration in question is not disturbed, and splitting of the macula is therefore found in field tests. Even after complete destruction or removal of one occipital lobe, macular splitting may be found in such tests if integration in the conscious visual area in use is not too greatly disturbed. These conditions would most likely obtain when the lobe destroyed was on the side opposite that of the conscious visual area.

This theory needs additional facts before it can be unreservedly accepted. Nevertheless, it seems sufficiently satisfactory to warrant the statement that the field determinations thus far made do not refute the evidence against bilateral occipital representation of the macula.

395 Commonwealth Avenue

⁹ Fuchs, W. (a) Untersuchungen über das Sehen des Hemianopiker und Hemiambyopiker, *Ztschr. f. Psychol.* **84** 67, 1920, (b) Eine Pseudofovea bei Hemianopikern, *Psychol. Forsch.* **1** 157, 1921.

PENICILLIN AND SULFADIAZINE

IN THE TREATMENT OF EXPERIMENTAL INTRAOCULAR INFECTION WITH
PNEUMOCOCCUS

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Diplococcus pneumoniae is considered the most frequent cause of severe intraocular infections following perforating injuries. Morax and Moreau,¹ A von Szily² and K Lindner³ stressed the importance of this organism in infections of penetrating wounds of the eye in modern warfare. Therefore the chemotherapy of experimental post-traumatic endophthalmitis caused by the pneumococcus was selected for the present study, which is the first part of more extensive investigations on the treatment of intraocular infections.

Statistical data on the types of pneumococci in cases of endophthalmitis and panophthalmitis following various perforating injuries are not available. Only in a few such cases have the types been identified according to Cooper's classification. It is justifiable, however, to apply to intraocular infections the statistical figures of the incidence of the various pneumococcal types present on the normal conjunctiva and isolated in external diseases of the eye, because it is assumed that the micro-organisms from the surface of the conjunctiva and cornea, drawn into the eye by the penetrating foreign body, generally become the source of infection. There was almost complete agreement among the investigators of different countries until 1938 that pneumococci in group IV of the former nomenclature were the most often found and were followed in incidence by strains of type III (Cheney, 1922⁴, Lundsgaard, 1925⁵, Vita, 1926⁶, Wright, 1927⁷, Clegg, 1927⁸, Lucic, 1927⁹, Lobeck, 1931¹⁰, Jahnke and Wamoscher, 1931¹¹, Schmelzer and Eckstein,

This study was supported by the Knapp Memorial Foundation

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From the Department of Ophthalmology of Columbia University College of Physicians and Surgeons and the Institute of Ophthalmology of Presbyterian Hospital

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10 Lobeck, E. *Zur Frage der Pneumokokken Infektionen im Auge*, Arch f Ophth **127** 395, 1931

11 Jahnke W, and Wamoscher L. *Zur Frage der Serumtherapie bei Pneumokokken-erkrankungen des Auges*, Ztschr f Augenh **74** 215, 1931

1934¹², McKee, 1935,¹³ and Spiratos, 1937¹⁴) In ophthalmology the first attempts to identify the twenty-nine higher types of the former group IV by agglutination reaction were carried out by Newman,¹⁵ Woods¹⁶ and Chamberlain¹⁷ These authors arrived, however, at slightly different conclusions Newman listed as most often found types VII, X and XXIII, Woods, types VII, XIV and XXIII and Chamberlain, types XIX, VI and XIV

Since in a few clinical cases of panophthalmitis types III, VII and X were reported as the cause of the infection and since these types are among those most frequently found on the surface of the eyeball, they were selected for inoculation into rabbits' eyes Furthermore, the effect of one of the drugs studied in experiments on rabbits was tested in vitro on the other frequently found types—namely types VI, XIV, XIX and XXIII

By injections of a dilution of a twenty-four hour broth culture into the anterior chamber of adult chinchilla rabbits a fairly well standardized infection with a typical course was obtained and used as the test object¹⁸ The action of two chemotherapeutic agents was studied sulfadiazine (2-[paraaminobenzenesulfonamido]-pyrimidine), as one of the newer sulfonamide compounds, and penicillin a product of the mold *Penicillium notatum*

PRELIMINARY EXPERIMENTS

The result of injection of different micro-organisms into the anterior chamber has been studied by several authors, notably by Picot,¹⁹ in 1898, who gave a good description of the clinical and anatomic changes, and by Venco²⁰ in his study on the effect of sulfonamide compounds on streptococcal and pneumococcal infections The techniques applied by these investigators were different from each other and also from that reported here In Picot's experiments no attempt was made to estimate the number of germs injected Venco used dilutions of a dried powder of pneumococci with an unknown number of viable germs In the experiments reported here this number was roughly estimated in each series by plate counts of appropriate dilutions of the broth culture in blood agar In the first part of the preliminary experiments the course of the inflammation after injection of the various types of pneumococci was observed The inflammatory signs, including excessive fibrinous or cellular exudation, usually reached their height in forty-eight to seventy-two hours With the strain of type VII a violent endophthalmitis with a massive

12 Schmelzer, H., and Eckstein, E. Die augenpathogene Bedeutung der Streptokokken und Pneumokokken (547 Untersuchungen), Arch f Ophth **132** 24, 1934

13 McKee, S. H. A Study of the Pneumococcus Group from the Inflamed Conjunctiva and Lacrimal Sac, Am J Ophth **18** 1021, 1935

14 Spiratos, S. Le pneumocoque, agent pathogene et saprophyte de l'oeil, Arch d'ophth **1** 589, 1937

15 Newman, E. W. Diplococcus Pneumoniae and Streptococcus Viridans in Ocular Diseases, Arch Ophth **19** 95 (Jan.) 1938

16 Woods, M. A. A Study of the Methemoglobin-Producing Organisms in Ocular Inflammations, Am J Ophth **22** 1111, 1939

17 Chamberlain, W. P., Jr. The Treatment of Pneumococcal Corneal Lesions with Sulfapyridine, Thesis, Columbia University Graduate School, 1940

18 Vaccination of the cornea with intracorneal injections was not satisfactory with our technic and culture material because of the frequent spontaneous regressions

19 Picot, V. Recherches experimentales sur l'inoculation de micro-organismes dans la chambre anterieur de l'oeil du lapin, Arch d'ophth **18** 341, 1898

20 Venco, L. Ricerche sulla attivita chemioterapica della para-aminofenilsulfamide nelle infezioni microbiche sperimentali dell'occhio, Ann di ottal e clin ocul **67** 179, 1939, Rilievi sperimentali sulla chemioterapia delle infezioni pneumococciche oculari mediante alcuni derivati organici dello zolfo, Arch di ottal **46** 307, 1939

exudate was observed within twelve hours. The character of the exudate and the sequence of the clinical changes varied somewhat with the strain of the pneumococcal type, but the inflammation generally led to suppuration of the anterior segment, perforation and phthisis bulbi or severe endophthalmitis followed by atrophy of the eyeball. Often in the later stages the cornea became partially or entirely infiltrated and vascularized. Of the 31 control eyes 1 healed spontaneously after a regression of iritis with hypopyon, and in another eye the infection did not take. The stages of the infection were routinely studied with the corneal microscope and slit lamp as long as massive exudate did not fill the anterior chamber. A large number of photographs were taken to illustrate the course of the infection.

On the basis of previous experiments on *Bacillus pyocyaneus* keratitis²¹ and clinical experience, sodium sulfadiazine was used iontophoretically in a 5 per cent solution. The amount of 0.25 Gm. per kilogram of body weight of sulfadiazine fed once daily was chosen to approximate the dose in human therapy. The second part of the preliminary experiments was concerned with the determination of the concentrations of the ammonium or sodium salt of penicillin²² best suited for local use. Solutions of 0.1 to 1.0 per cent were introduced by corneal baths and by iontophoresis²³. With both techniques solutions of 1.0 and 0.5 per cent damaged the epithelium and superficial layers of the cornea. Solutions of 0.25 per cent also damaged the epithelium to some extent when applied repeatedly by iontophoresis at 2 milliamperes for five minutes. The same concentration usually did not harm the cornea when applied frequently in a simple bath. A solution of 0.1 per cent could be employed with iontophoresis repeatedly with little or no damage to the epithelium. The two latter concentrations were therefore chosen for the experiments. The hydrogen ion concentration of these solutions was found to be between 7 and 8. The injurious action of the higher concentrations on the corneal epithelium has no parallel in the experiments on tissue cultures and on leukocytes reported by Florey and associates,²⁴ Thygeson²⁵ and others.

EXPERIMENTAL TECHNIC

The experiments were divided into two groups. In the first group a sharp 27 gage needle was inserted through the periphery of the cornea in a tangential direction, and 0.05 cc. of diluted broth culture of types III, VII or X was introduced into the anterior chamber. With this technic, visible loss of fluid rarely occurred after the withdrawal of the needle. In the second group the pupil was dilated with atropine sulfate solution, the anterior lens capsule injured with the needle and the aqueous permitted to escape. The needle was left in situ, and 0.07 cc. of the inoculum broth was then injected. Actually 0.05 cc. was introduced, since the measured capacity of the needle was 0.02 cc. In this group it was usually not possible to prevent the loss of an uncontrolled amount of fluid through the needle track in the cornea after the injection because the movement of the needle in the extensive slitting of the lens

21 von Sallmann, L. Sulfadiazine Iontophoresis in *Pyocyaneus* Infection of Rabbit Cornea, *Am J Ophth* **25** 1292, 1942.

22 Dr. Karl Meyer and his co-workers provided a regular supply of penicillin. It was prepared in his laboratory from the culture of *Penicillium notatum* by chloroform extraction and precipitation of the free acid by light purified petroleum benzine (Meyer, K., Chaffee, E., Hobby, G. L., Dawson, M. H., Schwenk, E., and Fleischer, G. On Penicillin, *Science* **96** 20, 1942). In most instances a weighed amount of the free acid was converted to the sodium salt by adding a drop of alcohol and finally dissolving the material in sodium bicarbonate-carbon dioxide buffer.

23 The technic of the corneal bath and that of iontophoresis were the same as those used in experiments on *B. pyocyaneus* keratitis²¹.

24 Florey, H. W., Abraham, E. P., Chain, E., Fletcher, C. M., Gardner, A. D., Heatley, N. G., and Jennings, M. A. Further Observations on Penicillin, *Lancet* **2** 177, 1941.

25 Thygeson, P. Personal communication, cited by Hobby, G., Meyer, K., and Chaffee, E. Chemotherapeutic Activity of Penicillin, *Proc Soc Exper Biol & Med* **250** 285, 1942.

capsule enlarged the opening All experiments and treatments were performed with the eye under anesthesia induced by 0.1 per cent nupercaine hydrochloride

The size of the inoculum as estimated by plate counts of appropriate dilutions of the broth culture in each series varied widely The minimal number of organisms injected was calculated to be 250 to 70,000 In general, 0.05 cc of a 10^{-4} dilution of a twenty-four hour broth culture was given The purity of the culture was repeatedly controlled by plating and the types with specific antisera The virulence of type III, which was used over a longer period, was increased several times by passage through mice

Treatment was started six and twelve hours after inoculation in the first group and six hours after inoculation in the second group The inflammatory symptoms after six hours in the first group varied, chiefly according to the number of organisms and the virulence of the strain, from the presence of a marked Tyndall sign and numerous circulating and deposited cells to that of fibrinous or cellular exudate which covered parts of the pupil and of the iris The signs twelve to thirteen hours after injection were generally those of a much more advanced iritis The inflammation due to type VII was especially violent In about 60 per cent of the experiments with this type the anterior chamber was almost completely filled with a fibrinous or gray opaque exudate at the time of the first treatment The severity of the infection was indicated by marked chemosis In 2 control experiments in which 0.05 cc of sterile broth was injected into the anterior chamber, a few cells were seen in the aqueous and on the surface of the lens for about twenty-four hours In the second group a fibrous net-

TABLE 1—Results of Sulfadiazine and Penicillin Treatment Begun Six Hours After Injection of *D. Pneumoniae* Types III and X

Treatment	Type of <i>D. Pneumoniae</i> Injected	Approximate Number of Organisms Injected	Number of Eyes	Period of Treatment	Number of Recoveries	Number of Temporary Improvements	Number of Losses
Sodium sulfadiazine iontophoresis and sulfadiazine feeding	III X	1,000 270 2,120	6 3 3	2-4 days 2-4 days 2-4 days	1	2	6 3
Control eyes—infused only by sulfadiazine given orally	III X	1,000 270 2,120	2 2 2	2-4 days 2-4 days 2-4 days			2 2 2
Sodium penicillin iontophoresis or bath	III X	1,000 270 2,120	5 3 3	2 days 2-3 days 2-3 days	5 3 3		
Control eyes—no treatment	III X	1,000 270 2,120	3 1 1				3 1 1

work covered the cataractous lens in 8 uninoculated control eyes as well as in the inoculated eyes However, in the latter the other signs of inflammation were generally fully developed In all instances in which the inflammation was unequal, the worse eye was treated and the better retained as a control

The severity of the clinical picture governed the period of treatment as well as the length and number of the iontophoretic applications and of the corneal baths In the six hour experiments one treatment of five minutes was given on the first day, repeated on the morning of the second day and supplemented by a three minute application in the afternoon In the twelve to thirteen hour experiments the eyes were treated twice on the day following the inoculation for five and three minutes, respectively Treatment was continued from two to six days in all experiments Generally the number of applications of penicillin and the application time were reduced on the second or third day, and further therapy depended on the response of the infection to the treatment As a rule equal numbers of eyes were treated in each series with the corneal bath, with ionization in which 0.01 per cent solution was used and with ionization in which 0.25 per cent solution was used In the second series of the infections with type VII, therapy starting twelve to thirteen hours after inoculation, only iontophoresis was employed

RESULTS

First Group—Table 1 shows that local application and oral administration of sulfadiazine started six hours after inoculation generally did not prevent the development of a severe endophthalmitis The high concentration of the drug in the aqueous attained with iontophoresis controlled the infection in several instances

for two to three days, but was evidently not effective enough after this period to prevent flare-ups which finally led to destruction of the eyeball. There were 3 exceptions. Of twelve eyes, in only 1, which received a small inoculum, did the inflammation clear up completely. In one rabbit the condition of both eyes improved considerably but an insidious iritis persisted. The 6 control eyes, which were influenced only by general treatment, suppurred. The results were the same with type III and type X.

Penicillin applied six hours after inoculation stopped the infection with types III and X in all instances—that is, in 11 eyes. No relapses occurred. The treatment was continued on the average of two to four days. The 5 control eyes were destroyed by the infection.

Table 2 presents the results of a series of experiments with types III, VII and X in which there was a lapse of twelve to thirteen hours between the inoculation and the treatment. No attempt was made to use sulfadiazine because of the unfavorable results at an earlier stage of the inflammation. In 25 of the 30 eyes

TABLE 2—Results of Penicillin Treatment Begun Twelve to Thirteen Hours After Injection of *D. Pneumoniae* (Types III, X and VII)

	Type of <i>D. Pneumoniae</i> Injected	Approximate Number of Organisms Injected	Number of Eyes	Period of Treatment	Number of Recoveries	Number of Losses
Treated Eyes						
	III	360	6	23 days	5	1
		1,360	6	23 days	6	
	X	4,300	6	3 days	5	1
	VII	1,500	6	5 days	5	1
		2,200	6	4 days	4	2
Totals			30		25	5
Control Eyes						
	III	360	1		1	
		1,360	2		1	1
	X	4,300	2			2
	VII	1,500	2			2
		2,200	2			2
Totals			9		2	7

in the series penicillin therapy was effective. In more than half of the eyes in the most advanced stages of endophthalmitis intensive treatment resulted in a final cure (fig 1), even when a transient rise in the intraocular pressure had increased the dimensions of the anterior segment of the eyeball. The ectasia bulbi regressed with the improvement of the inflammation, as the photographs in figure 2 show. In the lost eyes the endophthalmitis ran the following course. In an eye infected with type III and treated with a corneal bath the inflammation flared up on the third day and could not be controlled by more vigorous treatment. The second failure occurred in an eye which had received an inoculum of approximately 4,300 organisms of type X; iontophoretic treatment did not prevent the development of an abscess in the vitreous, and the eye was subsequently lost. In the 3 remaining eyes which were lost the violent inflammation caused by the very virulent strain of type VII was apparently too advanced to be improved by the therapy. Of 9 control eyes 7 were destroyed. In 1 control eye the infection did not take and in the other the iritis with hypopyon cleared up spontaneously.

Second Group—Because of the discouraging results with sulfadiazine in eyes without injury to the lens the experiments with traumatic cataract were confined to the penicillin treatment of eyes infected with types III and X. Of 12 eyes inocu-

lated with type III and treated with penicillin 3 were lost (table 3). The 3 failures belonged to the first tentative experiments carried out before it was learned that even if the inflammation appears checked macroscopically, intensive treatment should be continued for a few days. It is probable that these eyes could have been saved if iontophoretic treatment had been prolonged beyond the third

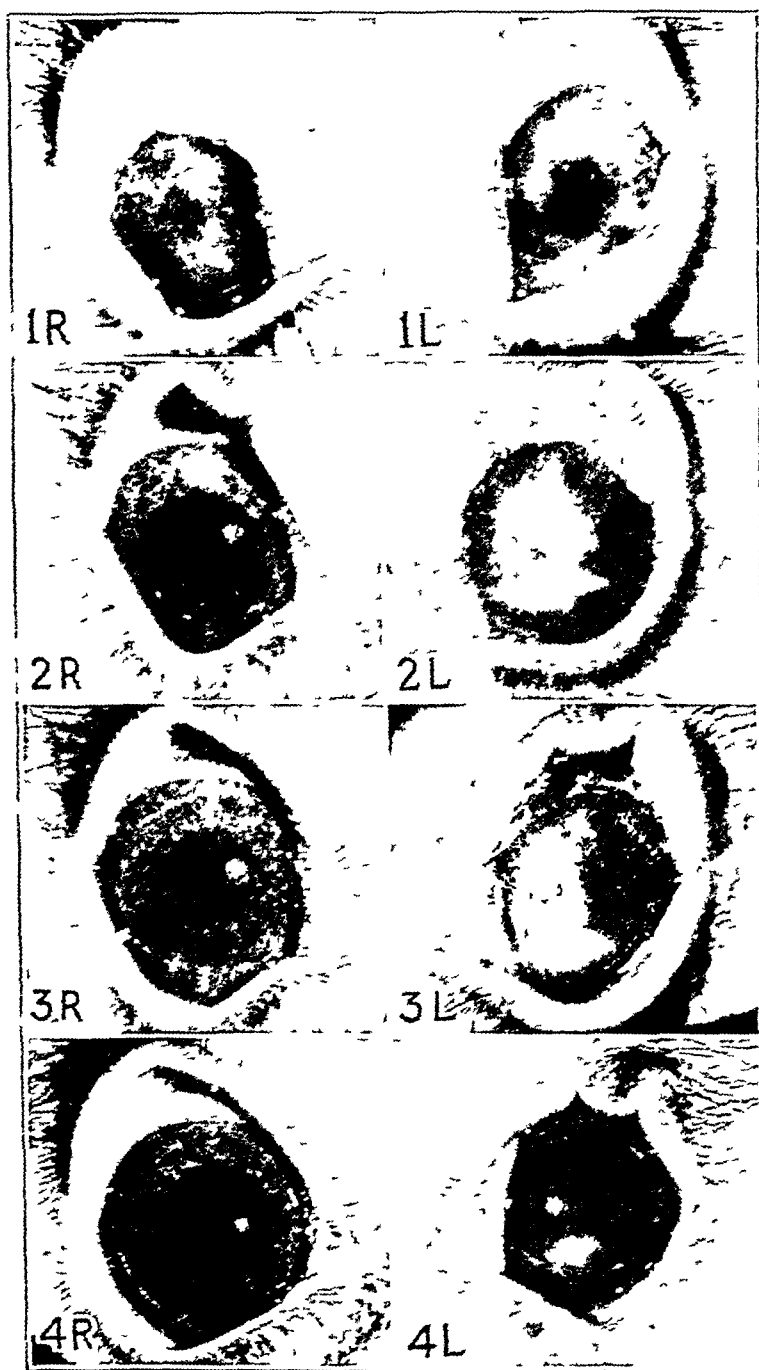


Fig. 1—Effect of penicillin treatment begun twelve hours after inoculation with *D. pneumoniae* of type VII. *R* indicates the treated and *L* the untreated eye, 1 *R* and 1 *L* were taken prior to the treatment and 2 *R* and 2 *L*, 3 *R* and 3 *L* and 4 *R* and 4 *L* after one, two and four weeks, respectively.

day. Three control eyes were lost in the usual course of infection. Excellent results were obtained in the 9 eyes inoculated with type X and treated with penicillin even though they presented advanced stages of infection and in 2 instances a fully developed endophthalmitis at the beginning of the treatment. Two of the

3 control eyes showed a stage of panophthalmitis after twenty-four hours, and all control eyes were destroyed

Experiments on Other Types—In order to consider the more frequently found types not studied in experiments on rabbits, types VI, XIV, XIX and XXIII were examined in vitro for their sensitivity to penicillin. Fleming's²⁶ dilution method was employed in accordance with Hobby's²⁷ demonstration of its superiority over the Oxford ring technic for sterile material. In all examined types growth was inhibited in the same range with the same sample of penicillin salt. The results did not differ appreciably from those obtained in vitro with types III and VII. Preparations of the penicillin salt routinely showed an activity of 0.15 to 0.3 microgram per cubic centimeter against 2,000,000 to 4,000,000 pneumococci of single strains of the various types.

COMMENT

Fleming, in 1929, first noted the antibacterial action of a strain of a *Penicillium notatum* against many gram-positive organisms. He called the active agent

TABLE 3—*Results of Penicillin Treatment Begun Six Hours After Injury of the Lens and Injection of D Pneumoniae (Types III and X)*

	Type of D Pneumoniae Injected	Approximate Number of Organisms Injected	Number of Eyes	Period of Treatment	Number of Recoveries	Number of Losses
Treated Eyes						
	III	800	6	4 days	3	3*
		960	6	4.5 days	6	
	X	42,000	6	5.6 days	6	
		75,000	3	5.6 days	3	
Totals			21		18	3
Control Eyes						
	III	800	2			2
		960	1			1
	X	42,000	2			2
		75,000	1			1
Totals			6		0	6

* One eye was treated by corneal bath, 1 iontophoretically with 0.1 per cent solution of penicillin salt and 1 iontophoretically with 0.25 per cent solution of penicillin salt.

penicillin and suggested its application to infections due to susceptible organisms. In the last three years the chemotherapeutic activity of penicillin was extensively studied in vitro and in vivo by several groups of investigators (Chain and associates,²⁸ Florey and collaborators²⁴ and Dawson and associates²⁹). Florey and his co-workers pointed out a great strain difference in the sensitivity of pneumococci to penicillin. Hobby and her collaborators³⁰ found that pneumococci were destroyed more rapidly than hemolytic streptococci. Among the studies of the clinical use of penicillin is the report of Florey and associates of the effective

26 Fleming, A. On the Antibacterial Action of Cultures of a *Penicillium*, with Special Reference to Their Use in the Isolation of B. Influenzae, *Brit J Exper Path* **10** 226, 1929.

27 Dr. Gladys Hobby gave practical advice in the application of this method.

28 Chain, E., Florey, H. W., Gardner, A. D., Jennings, M. A., Orr-Ewing, J., and Sanders, A. G. Penicillin as a Chemotherapeutic Agent, *Lancet* **2** 226, 1940.

29 Dawson, M. H., Hobby, G. L., Meyer, K., and Chaffee, E. Penicillin as a Chemotherapeutic Agent, *J Clin Investigation* **20** 434, 1941.

30 Hobby, G. L., Meyer, K., and Chaffee, E. Activity of Penicillin in Vitro, *Proc Soc Exper Biol & Med* **50** 277, 1942.

treatment of corneal ulcer in 2 cases and of conjunctivitis in 2 cases. So far as I know, other clinical or experimental observations on penicillin therapy of infections of the bulbus have not been published to date.

The results of the penicillin treatment of experimental intraocular infections with strains of pneumococci of types III, VII and X and the notable antibacterial

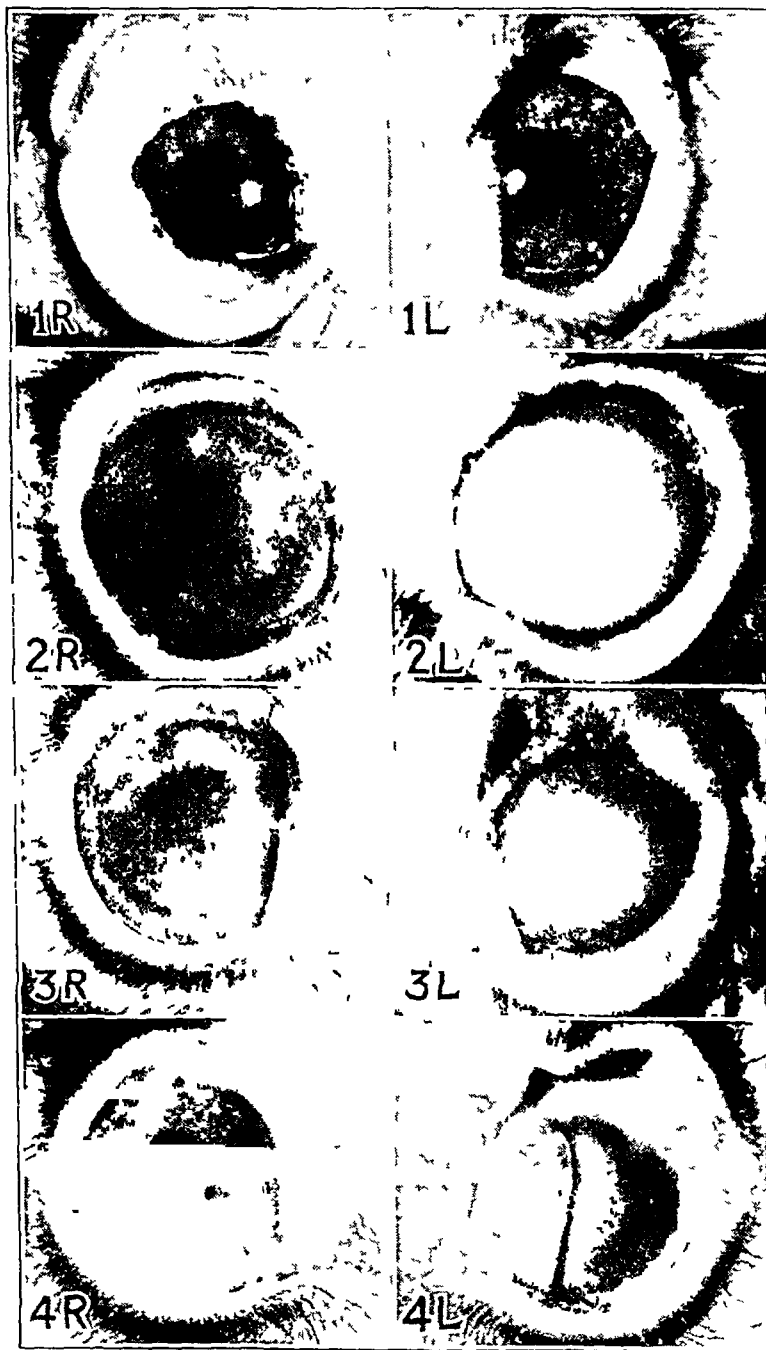


Fig 2—Effect of penicillin treatment begun twelve hours after inoculation with *D. pneumoniae* of type VII. *R* indicates the eye successfully treated despite development of secondary glaucoma with enlarged anterior segment and *L* the untreated eye. 1*R* and 1*L* were taken prior to treatment and 2*R* and 2*L*, 3*R* and 3*L* and 4*R* and 4*L* after one, two and four weeks, respectively.

action of penicillin in vitro on strains of the other types frequently found in the eye justify an optimistic point of view in regard to the clinical application of penicillin in the treatment of ocular pneumococcic infection. The activity of penicillin in severe pneumococcic endophthalmitis will be more appreciated when it is

compared with the failures of sulfadiazine treatment in the present series. These have their analogy in the unsatisfactory results of general sulfapyridine (2-[para-aminobenzenesulfonamido]-pyridine) therapy in experimental pneumococcal ulcers in rabbits as reported by Chamberlain³¹. Venco studied sulfonamide compounds in the treatment of experimental intraocular infections with pneumococci of types I, II and III. Treatment was begun at the time of infection, but the results in his small series can scarcely be evaluated, because of the questionable course in the control eyes.

The clinical effect of sulfapyridine treatment in 2 cases of pneumococcal ulcer was called of doubtful significance by Guyton and Woods³². In 4 of 6 cases of pneumococcal corneal ulcer observed by Chamberlain³¹ systemic treatment with sulfapyridine was apparently without effect, and in the remaining cases the results were not convincing. Bellows³³ mentioned 2 cases of pneumococcal serpent ulcer in which early chemotherapy with sulfonamide compounds did not stop the progression. On the other hand, the first favorable reports by Bailey and Saskin,³⁴ Roggenkampfer³⁵ and Rosengren³⁶ on the treatment of serpent ulcer with sulfonamide compounds cannot be judged adequately because of the absence of bacteriologic identification. In 1 case of pneumococcal endophthalmitis Guyton³⁷ found sulfanilamide therapy ineffective.

In some of the present series of experiments the initial good effect of the combined sulfadiazine treatment lasted for a few days. But usually a heavy exudate developed later and no further treatment could prevent the destruction of the eye. In a rabbit infected with type III, the inflammation became worse in spite of intensive sulfadiazine treatment of both eyes and feeding of sulfadiazine over a period of four days. Then penicillin was applied to the more severely affected eye. The iritis with hypopyon and other signs of inflammation cleared up after two treatments, and the eye returned to normal after six days. The other eye was destroyed by the infection. In a second rabbit combined sulfadiazine treatment greatly improved the inflammation in both eyes, but an insidious uveitis persisted, with numerous cells in the anterior chamber, swelling and hyperemia of the iris and posterior synechias. Two applications of penicillin to one eye nineteen days after inoculation and to the other thirty-five days after inoculation cleared the anterior chamber of the residual symptoms. Florey and his collaborators demonstrated the significant differences between the action of the sulfonamide compounds and penicillin. Of special bearing is the finding that hydrolytic protein breakdown products or products of tissue autolysis or pus do not affect to any appreciable degree the bacteriostatic action of penicillin, whereas they annul that of the sulfonamide compounds in vitro. Whether this difference, in addition to the higher bacteriostatic power of penicillin, explains the dissimilar effects of these two forms of chemotherapy in the eye cannot be decided.

31 Chamberlain, W. P., Jr. Treatment of Pneumococcal Corneal Lesions with Sulfapyridine. *Arch Ophth* **27** 869 (May) 1942.

32 Guyton, J. S. and Woods, A. C. Advances in the Use of Sulfanilamide Compounds in Ophthalmology, *Am J Ophth* **24** 428, 1941.

33 Bellows, J. G. Chemotherapy in Ophthalmology. *Tr Am Ophth Soc* **47** 19 1942.

34 Bailey, J. H., and Saskin, E. Treatment of Corneal Ulcer with Sulfanilamide, *Arch Ophth* **22** 89 (July) 1939.

35 Roggenkampfer, W. Hornhautulkus und Prontosil, *Klin Monatsbl f Augenh* **103** 211 1939.

36 Rosengren, B. Treatment of Ulcus Serpens Corneae with M & B 693, *Acta ophth* **17** 209, 1939.

37 Guyton, J. S. The Use of Sulfanilamide Compounds in Ophthalmology, *Am J Ophth* **22** 833, 1939.

Emphasis must be placed on the results of experiments with a twelve to thirteen hour interval between the inoculation and the first treatment with penicillin. At this time, in which the end of the logarithmic multiplication of the organisms would be reached *in vitro*, the structures of the anterior chamber show marked changes, such as swelling and hyperemia of the iris, massive exudate of plastic and fibinous type and synechias. Chemosis is often pronounced. In one eye in which perforation occurred after twenty-four hours, continued treatment led to an excellent result.

Half of the few trials of local treatment with penicillin carried out when the clinical picture of suppuration of the anterior segment developed or the anterior chamber was almost completely filled with exudate were without success. Two eyes with abscess of the vitreous also did not respond. In this connection it is of interest that the vitreous fluid of normal eyes after local application of penicillin did not demonstrate any bacteriostatic activity *in vitro*.

According to common clinical experience and the histologic observations of K. Lindner,³ the prognosis for post-traumatic intraocular infections is much less favorable when the lens is injured. In the experiments in which the lens was damaged (group II) the course of the inflammation was somewhat more serious than in the experiments with uncomplicated infections (group I), in which inoculation was followed by treatment after six hours. However, the endophthalmitis was less violent than expected, a factor which may be explained by the spontaneous healing of wounds of the capsule in rabbits with the formation of only a partial cataract.

In the first experiments infection of the "needle track" in the cornea frequently occurred, followed by an infiltration of various extensions twenty-four hours later in control eyes and in eyes treated with sulfadiazine. When penicillin treatment was used infiltration was not seen. These observations suggest the effectiveness of penicillin therapy in pneumococcal corneal infections.

Penicillin was introduced by corneal bath and by iontophoresis. Despite the much higher concentration found in the aqueous after iontophoresis, no essential difference was noticed in the effect of the two forms of therapy except when the inflammation was very severe. The number of failures was about the same with the two types of treatment, but generally the eyes with the more advanced infection were treated iontophoretically with a 0.25 per cent solution and the eyes with the mildest infection with corneal baths.

Both corneal bath and iontophoresis have several disadvantages in clinical application. For iontophoresis some equipment is necessary. This treatment with the Birkhäuser or van Heuven electrode cannot be applied without some cooperation from the patient. Children, therefore, cannot be treated repeatedly. In very painful eyes the pressure exerted by the tubes is not easily tolerated. It is probable that other forms of application, especially the use of wetting agents combined with penicillin, will be more satisfactory in these respects than the ionization method and corneal bath. However, preliminary experiments with three wetting agents—zephiran (a mixture of high molecular alkyl, dimethyl and benzyl ammonium chlorides), aerosol IB (dibutyl sodium sulfosuccinate) and penetrasol B (a mixture of aerosol IB, xylene, antipyrine and propylene glycol³⁸)—did not fulfil these expectations.

Further studies will show what concentrations of penicillin can be used in human eyes. In experiments on animals with severe infections the treatment

38 Herrmann, F., Sulzberger, M. B., and Baer, R. L. New Penetrating Vehicles and Their Solvents, *Science* **96** 451, 1942.

was continued twice daily even after an abrasion caused by previous iontophoretic treatments with 0.25 per cent solution had occurred. This epithelial damage healed in a few days without any residual opacity except in an eye in which a cloudy area remained in the center of the cornea for several weeks. The abrasions which occasionally were seen after repeated iontophoretic treatments with 0.1 per cent solution were small and healed in one day.

SUMMARY

1 Experimental intraocular infection caused by *D. pneumoniae*, type III and type X, was not stopped or was only temporarily improved by intensive local treatment with sodium sulfadiazine combined with sulfadiazine feeding when the treatment was initiated six hours after inoculation.

2 Severe intraocular infection caused by types III, X and VII was usually checked by local treatment with the sodium or the ammonium salt of penicillin in solutions of 0.25 per cent and 0.1 per cent even when this treatment did not start until twelve to thirteen hours after inoculation. The local applications were generally continued from two to four days.

3 Intraocular infection caused by the injection of types III and X with simultaneous injury of the lens capsule was treated successfully with penicillin in most instances in which the treatment was started six hours after injection and continued five to six days.

4 The iontophoretic introduction of the penicillin salt in 0.1 and 0.25 per cent solutions was occasionally more effective than the corneal bath (0.25 per cent solution) when the infection was very severe.

5 If repeated iontophoretic applications of 0.25 per cent solution were used because of the severity of the infection, corneal damage was noticed in the form of a large abrasion which usually healed without residual opacity after a few days.

6 Strains of types VI, XIV, XIX and XXIII showed in vitro the same sensitivity to penicillin as the strains of types III and VII used in the infection of eyes of rabbits.

Miss J. Di Grandi participated in all experiments and carried out the bacteriologic part of the study.

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COMBINED INTRACRANIAL AND ORBITAL OPERATION FOR RETINOBLASTOMA

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The purpose of this paper is to describe a new surgical approach for the treatment of retinoblastoma (glioma of the retina)

The results of enucleation of the eye in treatment of this tumor have been discouraging. An analysis of various series reported in the literature is shown in the accompanying table. The average survival rate even for short follow-up periods is only 18 per cent. If the reports of Hirschberg and Wintersteiner¹ are discounted as perhaps not in accord with the results of modern surgical technique, the statistics are somewhat less discouraging (a cure in 50 per cent of cases), although the most recent report of all is the least favorable (35 per cent of cures).

Results of Enucleation of the Eye for Retinoblastoma as Reported in the Literature

Date	Author	Follow Up, Years	Total Cases	Cures	
				Number	Percentage
1868	Hirschberg ^{1a}		75	4	5
1897	Wintersteiner ^{1b}	2	497	65	13
1911	Adam ^{1c}		46	26	57
1916	Leber ^{1d}		28	16	57
1941	Parkhill and Benedict ^{1e}	1	31	11	35
	Grand total		677	122	18
	Total for last three		105	53	50

What is widely recognized as true but often minimized in the discussion of retinoblastoma is the tendency of the tumor to invade the optic nerve early and to extend backward within the confines of the nerve sheath to the intracranial cavity. Here it may spread into the chiasm and opposite optic nerve. It invades contiguous brain and meninges and spreads widely via the subarachnoid space.

It must be stressed that the extension of the tumor into the optic nerve is the really important consideration. For it is this process that goes on unseen, defying recognition by the routine methods of examination and preceding, as a rule, any extension through the sclera into orbital tissues and blood-borne metastasis to distant organs.

Read before the Section of Ophthalmology, New York Academy of Medicine, April 19, 1943.

From the Department of Surgery of the New York Hospital and Cornell University Medical College.

1 (a) Hirschberg, J. Anatomisch Untersuchungen ueber Glioma Retinae, Arch f Ophth **14** 30, 1868. (b) Wintersteiner, H. Das Neuroepithelioma Retinae, Vienna, Franz Deuticke, 1897. (c) Adam, C. Statistisches, Klinisches und Anatomisches ueber das Glioma Retinae, Ztschr f Augenh **25** 330, 1911. (d) Leber, T. Die Geschwulstbildungen der Netzhaut, in Graefe, A., and Saemisch, E. T. Handbuch der gesamten Augenheilkunde, ed 2, Leipzig, Wilhelm Engelmann, 1916, vol 7, chap 5. (e) Parkhill, E. M., and Benedict, W. L. Gliomas of Retina. Histopathologic Study, Am J Ophth **24** 1354, 1941.

In an admirable study of 119 cases in which the eye had been enucleated for glioma (retinoblastoma) from which there had been "no extra ocular extension," Reese² showed that in 63 (or 52 per cent) there had been invasion of the optic nerve posterior to the lamina cribrosa and in 51 the operative section was distal to the extension of the tumor. In other words, the operation failed to remove the tumor in 43 per cent of the 119 cases. The study showed further that the size of the growth in the globe had no bearing on the presence or degree of extension in the nerve, and sometimes a relatively small retinal tumor was accompanied by neural extension.

It has been twenty years since Jean,³ writing about glioma of the retina (retinoblastoma), said, "It seems advisable that brain surgeons should attack these cases from within the brain [? skull] which they can do with reasonable safety." Yet since that time there have been reports of but two attempts at this approach to the treatment of retinoblastoma. It is the purpose of this presentation to reopen the discussion of the intracranial operation as part of a combined procedure for the cure of patients with retinoblastoma and to report 2 cases illustrating the advantages of the procedure.

Doubtless many patients having extension of the tumor into the optic nerve could be cured if enough of the nerve was resected in addition to enucleation of the eye. While it might be reasonably expected that sometimes nearly a centimeter of the nerve could be removed at the time of enucleation of the eye, actually the average length of the nerve found in Reese's study² was 3 mm. Some surgeons⁴ have advised exenteration of the orbit so that more of the nerve may be resected when its section at the time of enucleation has passed through tumor. This more radical operation, besides being grossly disfiguring, would often fall short of giving the desired result when the nerve was invaded farther proximally.

Irradiation has been employed for some time in the treatment of the initial tumor and the residual tumor in the optic nerve following enucleation. The recent report by Martin and Reese⁵ on the use of irradiation in the treatment of retinoblastoma is the most comprehensive statement to date on what can be expected from this form of treatment. These authors concluded that immediate enucleation of the eye is the safest plan if the tumor is unilateral. If both eyes are involved, with loss of vision, bilateral enucleation is the procedure of choice, although if any vision exists in one eye, they employ enucleation of the worse eye and irradiation of the other. The purposes for which irradiation is recommended are (1) treatment of early growths in an attempt to conserve vision in one eye and (2) treatment of postoperative residual or recurrent tumors.

Little can be expected from the irradiation of recurrent tumors that come to attention some time after enucleation of the eye. But the practice of employing irradiation promptly when microscopic examination of the enucleated eye reveals that tumor has invaded the optic nerve proximal to the point of operative section has much in its favor. Reese² and Martin and Reese⁶ have stressed the value of this plan of treatment and established dosages for the maximum irradiation to

2 Reese, A. B. Extension of Glioma (Retinoblastoma) into the Optic Nerve. *Arch Ophthalmol* 5: 269 (Feb.) 1931.

3 Jean, G. W. Discussion, *Arch Ophthalmol* 51: 505, 1922.

4 de Schweinitz, G. C. Diseases of the Eye, ed. 10, Philadelphia, W. B. Saunders Company, 1924, p. 536.

5 Martin, H. E., and Reese, A. B. Treatment of Retinoblastoma (Retinal Glioma) Surgically and by Irradiation, *Arch Ophthalmol* 27: 40 (Jan.) 1942.

6 Martin, H. E. and Reese, A. B. Treatment of Retinal Gliomas by Fractionated or Divided Dose Principle of Roentgen Radiation. Preliminary Report, *Arch Ophthalmol* 16: 733 (Nov.) 1936. footnote 5.

be employed. They recommended for both postoperative residual and recurrent growths the administration of 7,000 to 9,000 r over a three to four week period, followed by intraorbital implantation of radon seeds providing 5 to 10 millicuries. Their figures on a series of 6 cases show that if irradiation is instituted immediately after enucleation, when tumor is discovered in the remaining part of the resected optic nerve, the patient has a 66 per cent chance of cure. If growth of the tumor occurs after the initial course of therapy, no further irradiation can be given for fear of its causing necrosis, in fact, in 1 of their cases (case 20) fatal meningitis developed after exenteration of the orbit and implantation of radon seeds in the optic nerve.

While the results from enucleation of the eye combined with irradiation of the involved optic nerve stump are an improvement over those obtained from either enucleation or irradiation alone, there is justification for seeking methods that may provide still better results. It has not yet been made clear what the principal reasons are for failure in those patients who have had the combined treatment, but it may be surmised that many of the failures occur in those with neoplastic extension that has progressed to a point in the optic nerve where irradiation is not effective. From the beginning the obstacle in the path of cure of more patients with retinoblastoma has been the inability to remove surgically or affect adequately by irradiation that part of the invaded optic nerve that cannot be reached through the orbit.

The seemingly obvious adjunct to the routine procedures employed by the ophthalmologist is intracranial resection of the optic nerve. Jean⁷ lays the blame on the ophthalmologist for not seeking the aid of the neurosurgeon, but perhaps the latter is as much to blame for not taking some initiative in the matter.

The first recorded use of intracranial resection of the optic nerve invaded by a retinoblastoma is in the case of Dott and Meighan.⁸ The patient was a child of unspecified age in whom the tumor filled the enucleated eye though it did not traverse the sclera. But presumably tumor had been left in the optic nerve, since an "attempt" was made to remove more of the nerve through the orbit seven days after enucleation. Later radium was used, and still later the remainder of the optic nerve up to the chiasm was removed intracranially. "The region became infected but this later subsided," and the child's health was reported excellent one year later.

The other case of this kind is that reported by Rand⁹ in 1934. In a girl of 4 years and 7 months enucleation of the eye was followed by local recurrence of the tumor in the orbit, but an intact conjunctiva covered the tumor anteriorly. Through an intracranial approach the orbit was unroofed, the nerve resected back to the chiasm and the intraorbital mass removed. Accidental disruption of the conjunctiva anteriorly provided a portal for infection and a cerebrospinal fluid fistula through the orbit was followed by meningitis and death.

Bennett¹⁰ attempted avulsion of the optic nerve through the orbit, causing such trauma to the chiasm that postoperative hemianopsia developed in the remaining eye.

Perhaps these accounts afforded little incentive for other surgeons to attempt removal of the intracranial portion of the optic nerve, but it can hardly be said

7 Jean, G. W. Glioma of the Retina, Correspondence, J. A. M. A **100** 1793 (June 3) 1933.

8 Dott, N. M., and Meighan, S. Intracranial Resection of the Optic Nerve in Glioma Retinae, Am. J. Ophth. **16** 59, 1933.

9 Rand, C. W. Glioma of the Retina. Report of a Case with Intracranial Extension. Arch. Ophth. **11** 982 (June) 1934.

10 Bennett, H. P. Case of Primary Intradural Tumor of the Optic Nerve, Brit. M. J. **1** 1041, 1905.

that the circumstances in any of the cases were ideal for a good result. The use of the intracranial operation in conjunction with enucleation of the eye should be carefully planned in such a way as to avoid the two chief threats to a successful outcome, namely, incomplete removal of the tumor and serious infection.

It is believed that the following 2 cases demonstrate a relatively safe and promising combined procedure for the total removal of the eye and its optic nerve.

CASE 1—S W, a 6 month old girl, on the recommendation of Dr Irving J. Hausemann, was admitted to the New York Hospital in June 1942 because of recent convulsions. Her birth had been unremarkable and her development normal. The family history was not important. Some of the attacks were characterized by sudden turning of the head to the right, stiffening of all extremities and failure to respond. In other attacks the child would raise the arms over the head and become limp, so that the head would fall forward if she was held upright. At the same time she would turn the head aimlessly from side to side, stare vacantly and drool from the mouth. During these attacks, which lasted one to two minutes, there were no convulsive movements or cyanosis, and recovery was complete and prompt at the end of each attack. The attacks occurred from two to five times daily.

Examination revealed the baby to be healthy, with no abnormalities except a tumor of the right retina. Blood counts and chemical examinations of the blood gave normal results. The spinal fluid and roentgenograms of the skull were normal.

The right eye appeared to be normal in every way but for a rounded, elevated, grayish white mass in the retina to the temporal side of the optic disk. The mass was oval, apparently solid, well demarcated and slightly larger than the disk and had a fine capillary blood supply over its surface. The consensus of all the examiners, including several ophthalmologists and neurologists, was that the tumor was in all probability a retinoblastoma. Intracranial extension was considered a possible cause for the convulsions.

On July 10, with open mask ether anesthesia, a craniotomy was performed through a small, frontotemporal incision on the right. The brain and meninges exposed were normal in appearance. The right frontal lobe was elevated to expose the optic nerves and chiasm. These were normal in appearance, and that portion of the right optic nerve between the chiasm and the optic foramen was resected. The right optic foramen was plugged with a bit of muscle, and the wound was closed. But for moderate fever on the first two days the child's condition was excellent, and the postoperative course was uneventful.

The resected fragment of optic nerve measured 8 mm and failed to show any abnormality on microscopic examination.

On July 23, with open mask ether anesthesia, the right eye was enucleated. The conjunctiva was incised, and the extraocular muscles were divided at their insertions into the globe. After being freed from Tenon's capsule, the eyeball, together with the remaining portion of the optic nerve (about 1.5 cm), was lifted away with the enucleation spoon. The fascia was sutured posteriorly and Tenon's capsule sutured over a gold ball implant. The muscles were brought together with sutures in front of the implant, and the conjunctiva was closed.

The postoperative course was uneventful, and the child left the hospital in good condition ten days later.

Pathologic examination of the enucleated right eye showed an unusual type of glioma, which will be the subject of a separate report.

There is perhaps a point of debate about the exact nature of the retinal tumor in this case. In the six months since operation the child has had some convulsions, even with anticonvulsant medication, and epilepsy can definitely be diagnosed. The underlying cause may be tuberous sclerosis (epiloia), and the retinal tumor may be considered to have been related to this disease. However, the indications for enucleation of the eye had been definite enough in the beginning, and the two stage operation employed for total resection of the optic nerve, together with the removal of the eye, demonstrated the comparative ease and safety with which such operations can be performed.

CASE 2—S R, an 11 week old girl, referred by Dr Bernard Samuels and the New York Eye and Ear Infirmary, was admitted to the New York Hospital Dec 12, 1942. The child's birth and early development had been normal, but at the age of 6 weeks an unusual color of the right pupil was noted by the mother. A week later, when a physician was consulted, a diagnosis of retinal tumor of the right eye was made, and this was concurred in by all subsequent examiners.

Examination revealed the infant to be small, listless and somewhat undernourished looking. The head was moderately asymmetric and the scalp and face seborrheic. The abdomen was distended, and there was congenital deformity of some of the toes.

The right eye showed the characteristic changes due to a retinal tumor. The pupil gave a reddish yellow reflex, was dilated and did not react to light. The tumor filled the vitreous cavity, causing moderate secondary glaucoma and slight corneal edema. The left eye was normal.

After transfusion the child's condition seemed suitable for operation.

On December 15, with open mask ether anesthesia, a craniotomy was performed through a small, frontotemporal incision on the right side. The exposed meninges and brain were normal in appearance, as were the optic nerves and chiasm when seen after elevation of the frontal lobe. The intracranial portion of the optic nerve measured about 1 cm from optic foramen to chiasm, and this portion was resected. The stump of the distal fragment of the optic nerve was coagulated with the electrosurgical unit and the foramen plugged with a piece of muscle. The wound was carefully closed. There was moderate fever for the first two days after operation, but thereafter the course was uneventful.

The resected fragment of nerve measured 1 cm and failed to show any abnormality on microscopic examination.

On December 28, with open mask ether anesthesia, the right eye was enucleated. The conjunctiva was incised, and the extraocular muscles were divided at their insertions into the globe. After being freed from Tenon's capsule, the eyeball, together with the remaining optic nerve (about 1.5 cm), was lifted away with the enucleation spoon. Posterior and anterior purse string sutures closed Tenon's capsule over a gold ball implant. The muscles were brought together with sutures in front of the implant, and the conjunctiva was closed.

Pathologic examination showed that the eye was filled with a typical retinoblastoma which reached, but did not extend along, the optic nerve.

While the microscopic examination of the optic nerve did not show that the tumor had invaded the optic nerve, there was no way of predicting this prior to operation. The child's general condition was none too good to begin with, nevertheless both operations were carried out with minimal reaction. There is little experience to go on in judging the ability of an infant without intracranial disease to withstand intracranial operation, but resection of the optic nerve, judging from this and the previous case, should be attended by little morbidity or risk to life.

THE OPERATION

The intracranial operation is performed through a comparatively small cutaneous incision, like that routinely employed by neurosurgeons in the "hypophysial approach." It begins just in front of the ear and curves upward and forward to end at or just in front of the hairline of the forehead (fig 1, inset). The skin and galea are stripped from the temporal fascia and periosteum and retracted anteriorly. A small bone flap is made so that the anterior cut borders the supraorbital ridge as far laterally as possible, and the inferior cut is well down under the temporal muscle toward the zygoma. A little bone removed here with a rongeur after reflection of the flap facilitates the exposure. In infants the dura is adherent to the skull along the line of the coronal suture, which passes through the approximate center of the bone flap. Care must be taken, therefore, not to tear the dura or distort it unduly in elevating the bone.

The dura is opened by curving the incision just inside the anterior and temporal margins of the bony aperture. The posterior extent of the incision in the temporal region should traverse the middle meningeal artery, which requires coagulation or clipping. The frontal lobe is gradually retracted away from the floor of the frontal fossa, and the cisterna chiasmatis is evacuated. A good view of the optic nerve, chiasm and even the opposite nerve can be obtained without fear of damaging the brain, though special care must be taken to avoid injuring the olfactory nerves (fig 1 a).

The arachnoid is stripped away from the optic nerve and a small nerve hook passed under to free it all around and isolate it from the adjacent carotid artery, which lies partly beneath and lateral to the nerve (fig 1, *b*). The nerve is first transected at its junction with the chiasm. Then, while it is held on slight traction with a forceps, it is transected at the optic foramen. Neither of these sections is attended by more than slight vascular oozing, which can be controlled in the case of the chiasmal stump by light tamponade with a cotton pledget for a few moments. The ocular end of the nerve tends to retract into the foramen. Both the dural lining of the foramen and the nerve end are now coagulated by applying the electro-

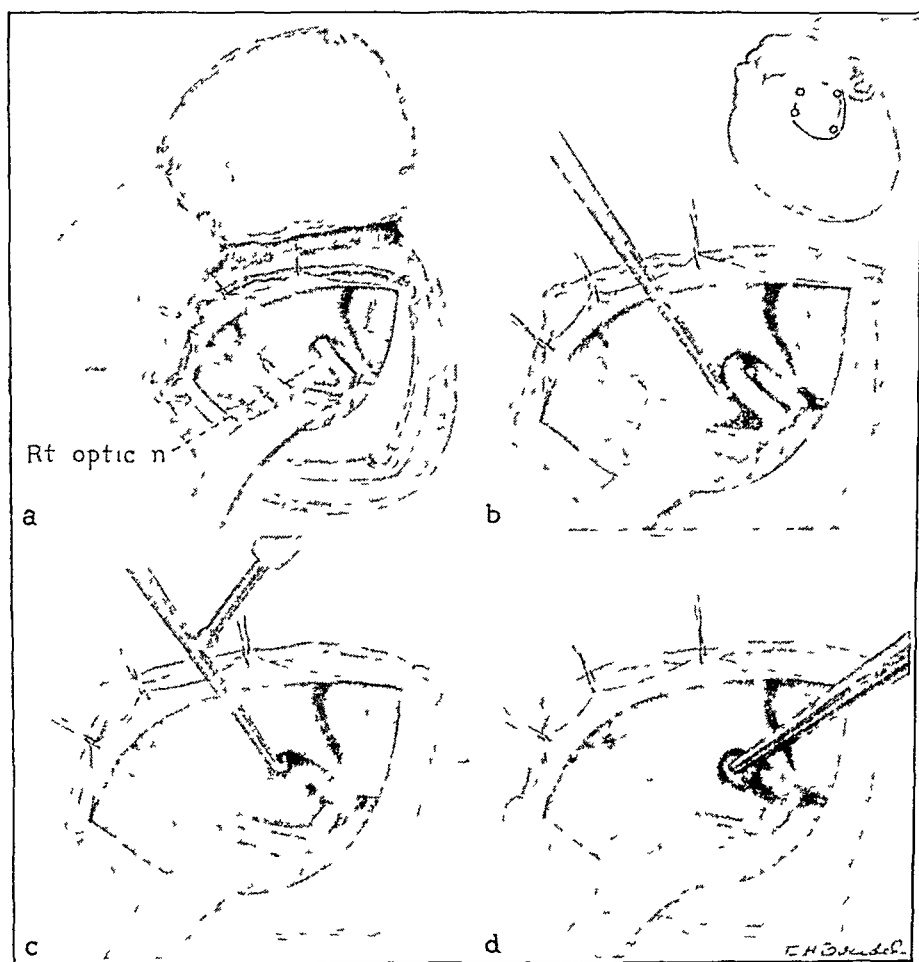


Fig 1 (case 2) —Operative sketches showing the intracranial resection of the optic nerve. The optic nerves, chiasm and adjacent structures are exposed by elevation of the frontal lobe of the brain (*a*). The optic nerve is freed from the optic foramen to the chiasm (*b*). The inset shows the incision on the scalp and outline of the bone flap. After resection of the optic nerve, the stump of the remaining nerve is coagulated in the foramen (*c*). The optic foramen is plugged with a piece of muscle to prevent leakage of cerebrospinal fluid after enucleation of the eye with the remaining portion of the nerve (*d*).

surgical unit to a metal nerve hook passed into the foramen (fig 1 *c*). A small piece of temporal muscle is firmly packed into the optic foramen to seal it off from the subarachnoid space (fig 1, *d*). An alternative method is to turn down a lappet of dura to cover the foraminal opening but this may be attended by some bleeding which is to be avoided if possible.

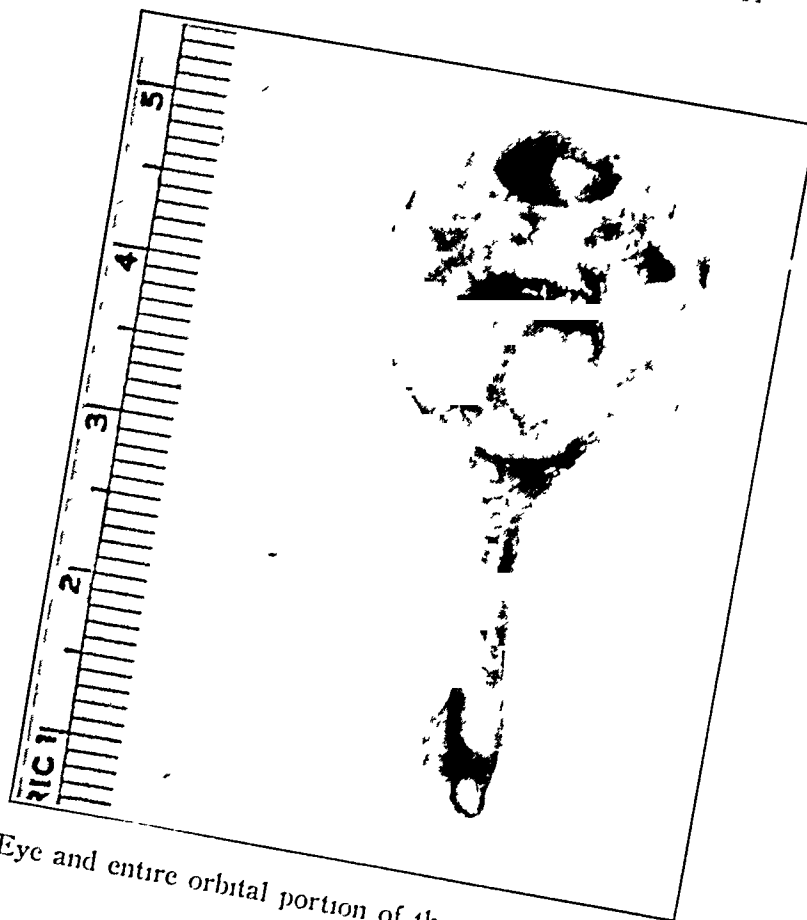


Fig 2 (case 2) —Eye and entire orbital portion of the optic nerve and nerve sheath removed in one piece

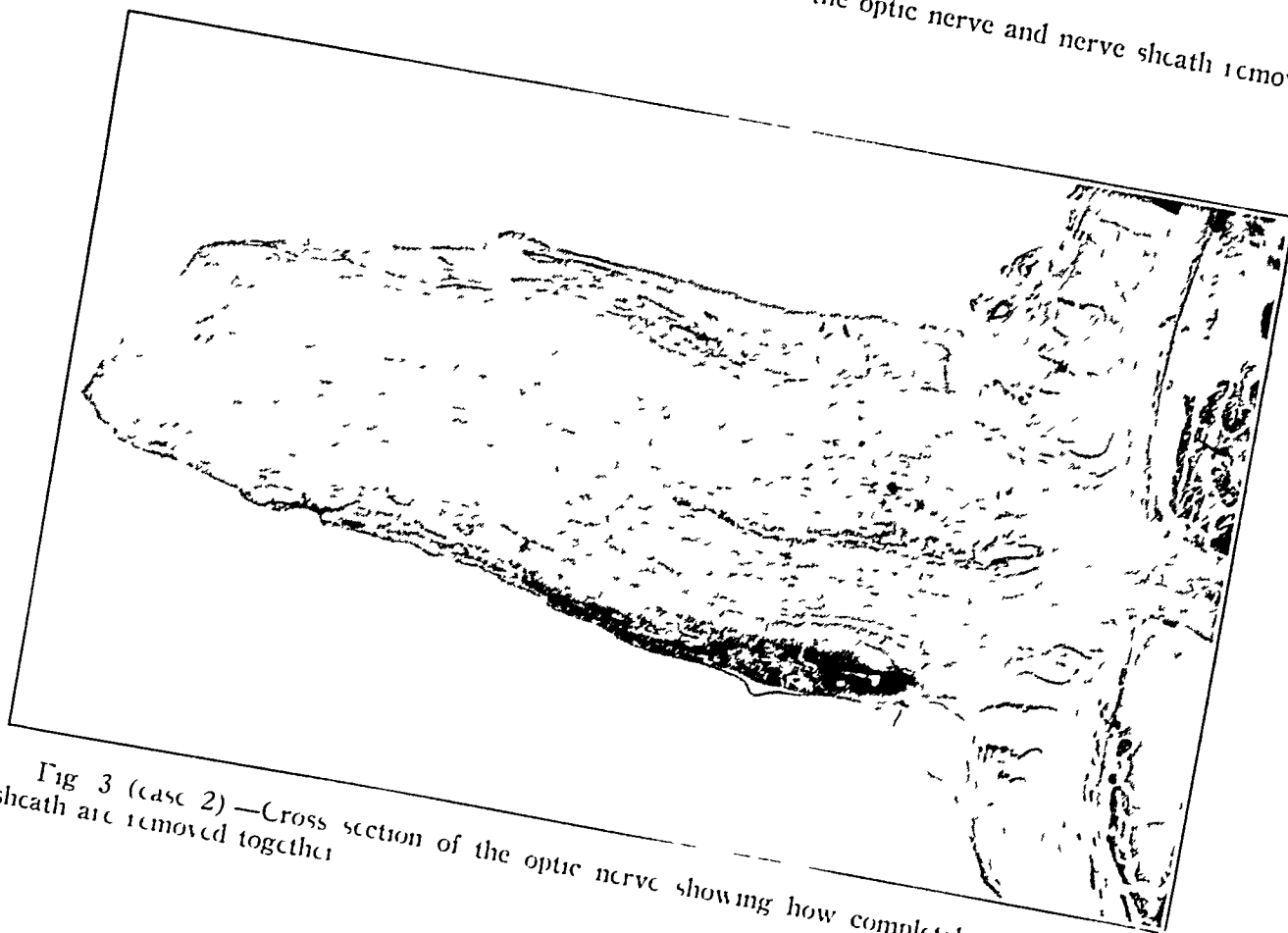


Fig 3 (case 2) —Cross section of the optic nerve showing how completely the nerve and sheath are removed together

In the closure, the dual margins are approximated and the replaced bone is held in position by one or two silk sutures passed through small drill holes. The temporal fascia, galea and skin are separately sutured with interrupted stitches of silk.

With infants and young children open mask ether anesthesia is preferable and an intravenous infusion of suitable fluids should be employed throughout and after the operation.

The secondary operation, enucleation of the eye with simultaneous removal of the remaining part of the nerve, has been carried out twelve and thirteen days later. It varies from the ordinary enucleation in a few particulars. All six extraocular muscles are tenotomized at their scleral insertions, but the optic nerve is not cut. Instead, an enucleation spoon is slipped behind the globe around the nerve, and the entire eye, optic nerve and nerve sheath are delivered intact by traction (fig. 2). Figure 3 shows how completely the optic nerve sheaths are removed with the nerve. Closure and prosthetic implantation are done in the usual manner. If too large a hole has been torn in Tenon's capsule posteriorly, a small purse string suture suffices to close it so that the implant will not slip out of position posteriorly.

COMMENT

The surgical procedure described is advocated in an effort to save that group of children who die from intracranial extension of retinoblastoma after inadequate treatment by enucleation of the eye. In spite of efforts to remove longer portions of the optic nerve by the orbital route, experience has shown that the operation of enucleation imposes limitations on the amount of nerve that can be resected. Reasons for avoiding exenteration of the orbit and for avoiding secondary intracranial operation have been given. The two choices remaining seem to be the procedure described here and that advocated by Martin and Reese. Experience with their method is still too limited for the drawing of sound, statistical conclusions. Since about half the eyes that are enucleated show extension down the nerve, and since immediate institution of heavy postoperative irradiation seems to save about two thirds of these, the expectation on the basis of present figures is about 80 to 85 per cent of cures. We cannot draw any statistical conclusions on the basis of our 2 cases. The relative merits of the two technics can be judged only when enough patients have been treated by each method and followed for a sufficient time thereafter. Some surgeons always prefer a radical surgical attack on malignant processes, others tend toward less radical surgical intervention plus irradiation. It might be added that in the treatment of retinoblastoma irradiation could still be employed after a radical surgical procedure, but the reverse would not be so safe or so satisfactory.

Perhaps the most important consideration in the proposed two stage operative removal of the eye and its entire nerve is the operative mortality to be expected. Doubtless until the contrary is proved it will be anticipated by many ophthalmologists that the mortality rate resulting from the procedure will outweigh the advantages. There are no statistics which are of assistance in predetermining the mortality rate, but it may be said that infants and young children on whom these operations will be performed stand simple intracranial operations, as well as successive operations, surprisingly well provided the necessary precautions in preoperative and postoperative care are employed. Two unnamed neurosurgeons cited by Jean¹ have stated that the risk of the intracranial resection of the optic nerve "should be very small," "2 per cent or thereabouts." We feel that the intra-

cranial operation should be attended by an operative mortality no greater than 5 per cent and probably considerably less than that

It might be possible on some of the older children for one to perform both the intracranial and the orbital operation at one time, thus avoiding the longer hospital stay and the slightly greater danger of two anesthetics. This method was recommended by Rand. However, two short operations should be better withstood by an infant than one longer and more extensive. Also, the sealing off of the optic foramen would be more nearly assured if a little time was allowed to elapse before the orbital part of the nerve was removed.

The practice of performing the intracranial resection of the nerve first has certain advantages and disadvantages. The chief disadvantage is that in about 50 per cent of the cases the operation will have been performed needlessly, that is, in those in which it is eventually found that any extension of the tumor into the nerve could have been readily removed at the time of enucleation. But it is certain that the difficulties of the operation and the dangers to life are considerably increased if the intracranial operation is resorted to after it has been discovered that tumor remains in the optic nerve after enucleation of the eye. There is the distinct danger of causing meningitis if the orbital portion of the nerve is pulled back into the cranial cavity after a recent enucleation in which there has been potential if not frank contamination of orbital tissues. There is the possibility that the nerve, considerably thickened by tumor, cannot be pulled back through its canal. In this case, unroofing of the canal and orbit would greatly add to the dangers of the operation. Also, any delay between the primary enucleation and secondary intracranial operation would make extension of any remaining tumor from the nerve into adjacent orbital tissues, or farther toward the brain, more of a possibility than it would be if the procedures were reversed. It is believed that coagulation of the stump of the optic nerve in its canal and plugging of the optic foramen as carried out in the initial intracranial operation will prevent intracranial extension of the tumor. In addition, coagulation of the nerve end should for a time prevent local extension of the tumor within the orbit. In short, the intracranial resection of the optic nerve as the initial operation has everything to recommend it except that in about half the cases it will have been performed needlessly.

The advisability of enucleation of both eyes in the presence of bilateral retinal tumor is perhaps debatable, but if it should be resorted to, both nerves could be resected intracranially at one preliminary operation.

SUMMARY AND CONCLUSION

In retinoblastoma the most important consideration is the extension of the tumor into the optic nerve. It is believed that in nearly 50 per cent of the cases the standard operation of enucleation of the eye is inadequate. Exenteration of the orbit, or secondary intracranial resection of the optic nerve, is unsatisfactory. The prompt irradiation of residual tumor in the optic nerve after enucleation has improved the results, however, the best results of this treatment fall short of cure in at least 15 to 20 per cent of cases.

It is proposed that a combined, or two stage, intracranial and orbital removal of the eye and the entire optic nerve offers the greatest possibility of cure in cases of retinoblastoma. Two cases of retinal tumor are reported in which this method of treatment was employed.

EXOPHTHALMOS DUE TO CHRONIC ORBITAL MYOSITIS

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The purpose of this paper is threefold first, to call attention to a comparatively rare type of chronic inflammation of the extraocular muscles known as idiopathic or primary chronic orbital myositis, second, to suggest a simple test for its detection, and, third, to report 4 cases studied at the Institute of Ophthalmology, Presbyterian Hospital, New York

By way of introduction it may be stated that chronic inflammatory or degenerative changes in the extraocular muscles have been reported in the following conditions (1) syphilis of the orbit, (2) tuberculosis of the orbit, (3) myasthenia gravis, muscular dystrophies and degenerative myositis of fatty, amyloid, vascular or traumatic origin, (4) exophthalmic goiter, before and after thyroidectomy, and (5) apparent good health (idiopathic form)

Because of the rarity of syphilitic and of tuberculous orbital myositis and the ease with which the correct diagnosis can usually be made, no attempt will be made to discuss these forms here The reader is referred to Offret,¹ who has reported in detail their clinical and pathologic characteristics Orbital myositis associated with myasthenia gravis and the muscular dystrophies, together with the rare degenerative types (fatty, amyloid, vascular or traumatic), will also be excluded from consideration

Reports of the histologic changes occurring in the extraocular muscles in exophthalmic goiter before thyroidectomy are rather few, but have been contributed by Moore,² Smelzer,³ Benedict,⁴ Wilson,⁵ Dudgeon and Urquhart,⁶ von Zalka,⁷ Friedenwald⁸ and others⁹ Most recent knowledge of such changes, however, has

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2 Moore, R F Exophthalmos and Limitation of Eye Movements in Graves' Disease, *Lancet* **2** 701, 1920

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4 Benedict, W L, and Knight, M S Inflammatory Pseudotumor of the Orbit, *Arch Ophth* **52** 582 (Nov) 1923

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6 Dudgeon, L S, and Urquhart, A L Lymphorrhages in the Muscles in Exophthalmic Goiter, *Brain* **49** 192, 1926

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8 Friedenwald, J S Orbital Myositis and Choked Disc in Exophthalmic Goiter, *Ann Surg* **96** 995, 1932

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come from cases of so-called malignant exophthalmos, which has been well described by Burch,¹⁰ Thomas and Woods,¹¹ Naffziger,¹² Ellett,¹³ Smelzer¹⁴ and others¹⁵

When one eliminates from discussion all cases of chronic orbital myositis of known cause there remains a small group of cases in which the cause is not known and the condition therefore merits the name of idiopathic, or primary, chronic orbital myositis

IDIOPATHIC CHRONIC ORBITAL MYOSITIS

Chronic orbital myositis of the primary type is a comparatively rare condition of the extraocular muscles of unknown cause. It is characterized histologically by lymphocytic infiltration, fibrosis and degeneration of muscle fibers. Grossly, the muscles are pale, enlarged and cartilaginous, and they cut with a gritty feeling. Clinically, it produces edema of the lids, exophthalmos and limitation of ocular motility.

This clinical and pathologic picture has been reported a number of times in the literature under a variety of names, for example, idiopathic myositis,¹⁴ orbital myositis,¹ Zenker's waxy degeneration,¹ pseudotumor¹ and exophthalmic ophthalmoplegia.¹⁵ Most case reports, however, have been published under the title of chronic orbital myositis (French), pseudotumor (German, English and American) or exophthalmic ophthalmoplegia (English).

According to Michail and Rusu,¹⁶ the first case report in the literature was made by Busse and Hochheim in 1903. These observers failed to note that Gleason,¹⁴ of this country, reported a case in the same year, fully describing the clinical and histologic observations. Since then a number of case reports, mostly in the French and German literature, have been added, generally under the title of pseudotumor. In 1909 Birch-Hirschfeld¹⁷ reviewed the literature on pseudotumor and added some case reports of his own. In 1923 Benedict and Knight⁴ were able to find only 5 additional case reports of pseudotumor, all of which were in the foreign literature.

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16 Michail, D., and Rusu, L. Les myosites des muscles periculaires, *Ann. d'ocul.* **177** 97, 1940.

17 Birch-Hirschfeld, A. Die Erkrankungen der Orbita, entzündliche Pseudotumoren, in Scheek, F., and Bruckner, A. *Kurzes Handbuch der Ophthalmologie*, Berlin, Julius Springer, 1930, vol. 3, p. 51. Diseases of the Orbit, in Graefe, A., and Saemisch, E. T. *Handbuch der gesamten Augenheilkunde*, ed. 2, Leipzig, Wilhelm Engelmann, 1930, vol. 9, pt. 1, chap. 13.

At that time they reported 6 cases, in 2 of which there was chronic nonspecific myositis. In 1925 Orlow¹⁸ collected 4 more case reports and added 1 of his own. He insisted that this type of myositis was distinct from syphilitic or tuberculous myositis and that it should be placed in a class by itself. In 1938, under the title of exophthalmic ophthalmoplegia, Brain and Turnbull¹⁵ reported their findings in a series of 31 cases, in some of which there were signs of hyperthyroidism. In 1939 Offret,¹ who had had some unhappy experiences with this condition (1 of his patients was a physician), published an excellent monograph on the subject. He had been able to collect and report on 34 cases, of which the myositis was of proved tuberculous origin in 6, of syphilitic origin in 5 and of unknown cause in 23.¹⁹ In 1940 Michail and Rusu¹⁶ reviewed 11 reported cases and added 2 of their own. In the same year Niall^{13a} presented an excellent paper on this subject and reported 11 cases (5 in detail), in some of which there was evidence of hyperthyroidism. Others who have contributed to this subject are Reese,²⁰ Samuels,²¹ O'Brien and Leinfelder,²² Williamson-Noble,²³ Colley,²⁴ Ellett,^{9b} Dalsgaard-Nielsen,²⁵ Schmencke,²⁶ Hine,²⁷ Franceschetti and Rutishauser,²⁸ Sautter²⁹ and others.³⁰

18 Orlow, K. Zur Pathogenese der Pseudotumoren der Orbitas. Myositis fibrosa der ausseren Muskeln der beiden Augen, *Monatschr f Augenh* **39** 460, 1925

19 Of these 23 cases, there had been microscopic studies in only 14 to prove the presence of myositis. In the remaining 9 cases the clinical picture of a tumor of the orbit was presented but at operation no tumor but only chronic inflammation was found. Had a biopsy specimen of the extraocular muscles been taken at the time of operation, the presence of orbital myositis might have been proved in many of these cases also.

20 Reese, A. B. Etiology of Exophthalmos, *Tr Am Acad Ophth* **39** 65, 1934, *Unilateral Exophthalmos and Its Surgical Treatment*, Pennsylvania M J **43** 605, 1940, *Exophthalmos Its Pathology and Ocular Manifestations*, New York State J Med **33** 73, 1933

21 Samuels, B. Some Notes on Orbital Tumors, *Arch Ophth* **7** 868 (June) 1932

22 O'Brien, C. S., and Leinfelder, P. J. Unilateral Exophthalmos, *Am J Ophth* **18** 125, 1925

23 Williamson-Noble, F. A. Inflammatory Pseudotumor of the Orbit, *Brit J Ophth* **10** 65, 1926

24 Colley, T. Inflammatory Pseudotumor of the Orbit. Case Report, *Brit J Ophth* **19** 93, 1935

25 Dalsgaard-Nielsen, E. Pseudotumor orbitae, *Acta ophth* **17** 418, 1939

26 Schmencke, A. Beitrag zur Histologie der "entzündlichen Pseudotumor," *Klin Monatsbl f Augenh* **76** 207, 1926

27 Hine, M. L. An Extra-Dural Tumor of the Optic Nerve, *Tr Ophth Soc U Kingdom* **42** 181, 1922

28 Franceschetti, A., and Rutishauser, E. Die entzündlichen Pseudotumoren der Orbita, *Arch f Ophth* **137** 93, 1937

29 Sautter, H. Pseudotumor der Orbita, *Klin Monatsbl f Augenh* **100** 29, 1938

30 During a cursory review of the literature on exophthalmos, it soon became obvious that a number of writers may have reported this condition under other titles, thus making a complete review of the subject almost impossible. Then, too, a number of observers gave excellent clinical and gross pathologic reports but failed to describe the histologic character of the extraocular muscles, thus making it impossible for us to learn whether chronic myositis was present. Abstracted material was used when the original articles were not available. This fact may account for our failure to find pathologic reports in some cases. (a) Pollems, W. Ueber tumorformige Amyloidosis in der Orbita, *Arch f Ophth* **101** 346, 1920. (b) Pines, B. Ein Fall von beiderseitiger entzündlicher Geschwulst der Augenhöhle (Pseudotumor), *Klin ocnia* **6** 116, 1928, abstracted, *Zentralbl f d ges Ophth* **21** 117, 1929. (c) Marbarx, and Van Duyse, D. Pseudoblastome de l'orbite, *Arch d'opht* **39** 466, 1921. (d) Imanishi, T. Ueber die entzündliche lymphomatose der Orbita, abstracted, *Klin Monatsbl f Augenh* **70** 281, 1922. (e) Huber, O. Ein Fall von entzündlichen Pseudotumor der Orbita, *ibid* **65** 718, 1920. (f) Tauferová-Karaskova, J. Inflammatory Pseudotumors of Orbit, abstracted, *Zentralbl f d ges Ophth* **26** 827, 1932. (g) Seka, W. A. Pseudotumor der Orbita, abstracted,

Of the three names used to describe the disease (chronic orbital myositis, exophthalmic ophthalmoplegia and pseudotumor), chronic orbital myositis is undoubtedly the best, because it represents a definite pathologic and histologic entity. The clinical term exophthalmic ophthalmoplegia was coined by Brian because he believed that the extreme swelling of the tissues of the orbit produced both the exophthalmos and the ophthalmoplegia. Pseudotumor is perhaps the poorest term, because it denotes so many different pathologic conditions. It was first used by Blich-Hirschfeld¹⁷ to describe exophthalmos in which no tumor was demonstrable. He classified cases of pseudotumor into three groups.

Group I consisted of cases in which the cardinal signs of orbital tumor (exophthalmos, displacement and disturbed motility of the globe) were present but the exophthalmos was cured by medical means, such as use of potassium iodide, mercury or quinine. The exophthalmos in these cases was supposed to be of syphilitic, tuberculous or hematogenous causation in spite of the fact that all known tests failed to substantiate the presence of any of the conditions suspected.

Group II included cases of exophthalmos in which the clinical diagnosis was orbital tumor but in which no tumor was found at operation. This group must have included some cases of exophthalmos due to thyroid disease, varicose veins of the orbit, diffuse lymphoblastoma, and so on.

Group III comprised cases of exophthalmos in which an operation revealed an abnormal orbital mass which on histologic study proved to be a chronic inflammatory process of a nonspecific nature containing diffuse follicular areas. A review of the case reports of this group indicates that it should be subdivided into (1) cases

Klin Monatsbl f Augenh **85** 426, 1930 (h) Israel, C. Apropos d'un cas de pseudo-tumeur inflammatoire de l'orbite, Bull Soc d'opht de Paris **50** 388, 1938 (In this article 79 cases have been collected from the literature) (i) Bruckner, A. Zur Klinik der Orbital-erkrankungen, Klin Monatsbl f Augenh **93** 104, 1934 (j) Morax, V, and Rousseau, F. Un cas de neoformation orbitaire d'interpretation difficile, Ann d'ocul **172** 41, 1935, abstracted, Zentralbl f d ges Ophth **34** 164, 1935 (k) Pincus, L. Primare Fettnekrose (Lipogranulomatosis) der Orbita, Klin Monatsbl f Augenh **94** 369, 1935 (l) Klitzsch, H. Pseudotumor der Orbita, ibid **93** 553, 1934 (m) Kalt, M. Tumeur orbitaire bilatérale avec double exophthalmic guerie par un traitement mercuriel, Arch d'opht **52** 655, 1935 (n) Soria, M. Pseudotumor der orbita, Arch de oftal hispano-am **36** 310, 1936, abstracted, Zentralbl f d ges Ophth **37** 291, 1937 (o) Braun, G. Pseudotumor der Orbita, Klin Monatsbl f Augenh **101** 434, 1938 (p) Tano, Y. Pseudotumor of Orbit, Acta Soc ophth jap (supp) **41** 760, 1937, abstracted, Zentralbl f d ges Ophth **40** 590, 1938 (In this article 12 cases have been collected) (q) Stargardt, K, cited by Dalsgaard-Nielsen²⁵ (r) Nakayasu, S. Acta Soc ophth jap **39** 325, 1935, abstracted, Zentralbl f d ges Ophth **34** 337, 1935 (s) Hirai, S. Inflammatory Pseudotumor Penetrating the Floor of the Orbit, Acta Soc ophth jap **41** 2162, 1937, abstracted, Zentralbl f d ges Ophth **41** 254, 1938 (t) Franklin, W S, and Cordes, F C. An Unusual Orbital Tumor, Tr Sect Ophth, A M A, 1922, p 243 (u) Kokott. Symmetrische Humoren der Orbita, Klin Monatsbl f Augenh **98** 373, 1937 (v) Schreck, E. Zur Klinik und pathologischen Anatomie der orbital tumoren, ibid **103** 1, 1939 (w) Lewis, P M. Inflammatory Pseudotumor of Orbit. Report of Case, Am J Ophth **21** 991, 1938 (x) La Rocca, V. Pseudo-Orbital Tumor in Diabetes, M Rec **141** 338, 1935 (y) de Schweinitz, G E. Concerning Certain Tumors of the Orbit and Certain Conditions Simulating Neoplasms of the Orbit, Tr Am Ophth Soc, 1911, p 842 (z) Joy, H H. Exophthalmos—Its Ocular Symptoms, New York State J. Med **33** 63, 1933 (a') Thomsen, H. A Case of Exophthalmos Caused by Chronic Inflammation (Pseudotumor). Postoperative Papilledema of Other Eye, Acta ophth **1** 248, 1923 (b') Hardy, G, and Hardy, W F. Preliminary Report on Orbital Tumors, Am J Ophth **17** 18, 1934 (c') Lemoine, A N. Pseudotumors of Orbit (Inflammatory), J Missouri M A. **38** 15, 1941 (d') McGregor, H G. Exophthalmic Ophthalmoplegia, Lancet **2** 579, 1940 (e') Jensen, V A. Malignant Exophthalmos After Strumectomy, Acta ophth **18** 1, 1940 (f') Duthie, O M. Exophthalmic Ophthalmoplegia, Tr Ophth Soc U Kingdom (pt 1) **59** 426, 1939

in which the extraocular muscles were chiefly or primarily involved and (2) those in which the muscles were spared and only the orbital fat was affected³¹

From this classification it is obvious that the term pseudotumor represents a number of different pathologic conditions, and that this diagnosis only covers up ignorance of the exact pathologic nature of the disease process in the orbit. This term should be employed only as a clinical diagnosis, and then only when a histologic study of the orbital pathologic changes is impossible. When microscopic material is available for study, a more specific histologic diagnosis should be made. Such histologic studies must be forthcoming if the confusion surrounding this diagnosis is to be clarified.

REPORT OF CASES

CASE 1—In March 1936 Mrs. R. D., a housewife aged 37, came to the Institute of Ophthalmology complaining of exophthalmos on the left side and diplopia of seven months' duration. She stated that the onset of her symptoms had been gradual and that for a time she had been able to overcome her diplopia by tilting her head backward. Later it had become necessary to keep the left eye covered to avoid diplopia and nausea. She had noticed no pain, visual impairment, edema or inflammation about her eyes except for swelling of the left eye following a bump over the left temple six months before she entered the hospital. Some time after the accident her left eye began to protrude.

Her past medical history was essentially irrelevant. There was no history of hyperthyroidism. After the birth of her daughter fifteen years before she had been told she had



Fig. 1 (case 1)—The eyes before operation. The patient was looking straight ahead with the right eye fixing.

nephritis and advised not to become pregnant again. Six years and again four years before she had been delivered of a stillborn infant and had subsequently suffered from nephritis and edema of the legs.

Examination showed her vision to be 20/20 in the right and 20/30 in the left eye. Her lids, conjunctivas, lacrimal sacs, intraocular tension and fundi were essentially normal. A slight ptosis was noted in the left eye. This eye was directed downward 15 degrees of arc and outward 5 degrees of arc. The patient was unable to elevate it above the horizontal plane. Readings on the exophthalmometer were 18 mm for the right and 20 mm for the left eye (fig. 1).

A report from her physician stated that the results of all her examinations and tests had been negative. In the hospital a routine urinalysis gave negative results, as did a Wassermann test of the blood. The spinal fluid chemistry and cell count were normal. The colloidal gold curve was normal. General physical and neurologic examination disclosed nothing significant. A roentgenogram of the left orbit showed increased soft tissue density and slight evidence of increased intraorbital pressure. The basal metabolic rate was +4 per cent.

³¹ There may be no justification for dividing Birch-Hirschfeld's third group into two subgroups, since the nature of the tissue change is histologically the same whether the orbital fat or the extraocular muscles are involved. A number of cases of pseudotumor have been reported, however, in which no mention was made of an abnormal state of the extraocular muscles or of their histologic character. Failure of the surgeon to remove a biopsy specimen of the orbital muscles along with the tumor mass found in the orbit may account for the apparent lack of muscle changes in such cases. It is therefore possible that in all cases of Birch-Hirschfeld's third group of pseudotumor, the orbital muscles were involved at least to some extent.

An intraorbital neoplasm was suspected and an exploratory operation of the left orbit through a lateral canthotomy done. The upper part of the orbit was normal, but below the globe a tumor was found running along the floor of the orbit from the globe to the apex. This growth seemed to infiltrate the inferior rectus muscle and was loosely attached to the periosteum of the orbital floor. It was about the size of a walnut, was fibrous and seemed to be encapsulated posteriorly. The surgeon noted that "undoubtedly by its check action on the inferior rectus muscle the tumor limited upward rotation of the globe." An attempt was made to remove the growth and at the same time save the inferior rectus muscle. The growth involved the muscle so intimately, however, that it was necessary to remove the muscle along with the tumor. Healing occurred without complications, and the patient left the hospital shortly. Follow-up examination four years later showed that the patient still had diplopia, the left pupil was dilated and reacted sluggishly to light. All movements of the extraocular muscles were limited, especially nasalward and downward.



Fig 2 (case 1)—Lymphocytes, fibrosis and muscle fiber degeneration ($\times 200$)

The pathologic report stated that the process consisted of chronic inflammation with degeneration of the muscle fibers. The histologic diagnosis was chronic inflammation and idiopathic myositis, or Zenker's waxy degeneration (fig 2).

CASE 2—In July 1939, I. M., aged 55, a merchant, presented himself for examination because of diplopia and inability to elevate his right eye (fig 3A). His difficulty had begun seven months before with diplopia and turning downward of the right eye. He complained of no pain or inflammation in his eyes. His vision was good in each eye, but in order to see straight ahead with the right eye he had to tilt his head backward. His general health was good.

The patient's history disclosed chronic sinus disease, for which he had had the middle turbinate bone removed in 1916 and an operation on the frontal sinus in 1919. In 1933 he had an attack of benzene poisoning and a spontaneous pneumothorax of the right lung which was considered to be of unknown causation. This cleared up spontaneously in a few months.

A number of roentgenograms of the chest taken at that time showed an old bilateral healed pulmonary tuberculosis with thick fibrosis and small calcifications in the apex of the upper lobe of the right lung. Roentgenograms of the chest taken yearly to the time of writing have not changed this diagnosis and have shown no recent infiltration of either pulmonary field. There was no history of thyroid disease.

Two of the patient's brothers were said to have retinitis pigmentosa, and the son, aged 24, was said to have bilateral central scotomas and optic nerve atrophy due to macular changes, perhaps of a tuberculous inflammatory process.³²

Examination showed the patient's vision to be 20/20—3 in the right eye and 20/20—2 in the left with a correction of +1.00 D sph \subset 0.50 D cyl, axis 100 before each eye. The lids, conjunctivas, lacrimal sacs and fundi were essentially normal. Examination of the extraocular muscles gave a first impression of a paralysis of elevation associated with exophthalmos on the right side. All movements of the left eye appeared normal. The right eye was turned directly downward about 25 degrees of arc, and the patient was unable to elevate the globe even so much as 5 degrees from this fixed position. Closer examination of the rotations of the right eye showed that all the extraocular muscles of this eye were active except the superior rectus muscle. The inferior oblique muscle was unable to elevate the fixed globe, but it was able to rotate the globe outward when the patient was asked to look up and to the left. The levator function was intact, and no ptosis was present, in fact, there

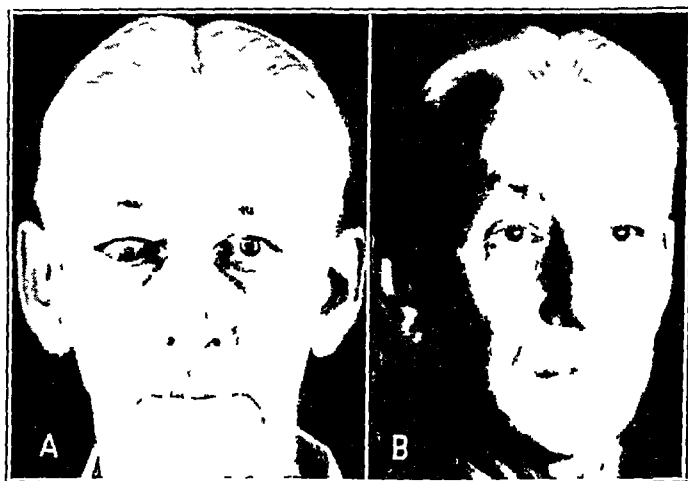


Fig 3 (case 2)—A, the patient before operation, looking straight ahead with the left eye fixing. B, the patient after operation, looking straight ahead with both eyes fixing.

seemed to be an overaction of the right levator muscle, which accentuated the apparent exophthalmos and produced a frightened staring expression (fig 3A).

Because the observations on the muscles did not correspond with those in most cases of paralysis of the superior rectus muscle, some inflammatory process binding the globe down to the floor of the orbit was suspected. A wisp of cotton saturated with 10 per cent cocaine hydrochloride was inserted in the inferior cul-de-sac to effect deep local anesthesia. A fixation forceps was then applied to the tendon of the inferior rectus muscle and gentle traction exerted to rotate the globe upward. This met with firm resistance, and it was impossible to elevate the globe even so much as 10 degrees of arc. This condition was thought to be due to some inflammatory or neoplastic process binding the globe or the inferior rectus muscle down to the floor of the orbit.

Since the right eye was fixed in a downward position of gaze, it was necessary to have the patient tilt his chin upward until the two corneas were on the same plane in order to get the exophthalmometer readings. These were 15 mm for each eye. Had it been possible to take these measurements in the usual manner, there is little doubt that an exophthalmos of 2 or 3 mm at least would have been recorded.

A general physical examination revealed only vitiligo of the face and both arms. The Mantoux test gave a reaction of 2 plus, and a roentgenogram of the chest showed bilateral healed pulmonary tuberculosis with calcification and fibrosis in the apex of the right lung. The basal metabolic rate was +16. The Wassermann reaction of the blood was negative,

32 Eagleton, W. P. Personal communication to the authors.

a routine blood count and differential count were normal, and routine urinalysis gave negative results. A roentgenogram of the orbits and optic canals revealed only a slight increase in soft tissue density of the right orbit, with nothing to indicate its cause.

Because it was thought that some chronic inflammatory or neoplastic process was binding the globe down to the floor of the orbit, the orbit was explored through a lateral canthotomy in August 1939. A solid, fibrous, smooth, firm, dark bluish mass below the globe, which seemed to be attached to all sides of the inferior rectus muscle, was observed. The mass began 5 or 6 mm from the insertion of the inferior rectus muscle to the globe and extended to the apex of the orbit. The growth was estimated to be 30 mm long, 8 to 10 mm thick and 10 to 12 mm wide. It cut with difficulty with scissors and was removed in five pieces. We wished to save as much of the inferior rectus muscle as possible. But no normal tissue of this muscle was noted, and at the conclusion of the operation almost all of the tumor



Fig 4 (case 2)—Lymphocytes, fibrosis and muscle fiber degeneration ($\times 200$)

mass and the inferior rectus muscle had been removed. The optic nerve, floor of the orbit, globe and the other rectus muscles appeared to be normal to palpation. At the conclusion of the operation the globe was freely movable. The wound was closed without drainage. The patient made an uneventful recovery.

Since the operation the patient has been able to move his right eye moderately from side to side but not below the horizontal plane. With his head tilted forward about 10 degrees of arc he has single binocular vision, and when he looks downward, the right upper lid covers the pupil so that he does not see double. His vision is 20/20 in each eye, and his fundi and pupillary reactions are normal. The patient does not wear an occluder now and asserts that he is more comfortable than before operation (fig 3 B).

Dr A. B. Reese's pathologic report stated: "The specimens contained considerable connective tissue and degenerated striated muscle fibers which were undergoing fibrosis. Scattered through the tissue were numerous irregular focal areas of inflammation containing large numbers of lymphocytes and a few plasma cells. Within and surrounding these inflammatory areas there were degeneration and destruction of muscle tissue, some of the muscle fibers

showed swelling and loss of striae. In some regions inflammatory cells were closely packed together in almost solid masses. In other areas there was a looser arrangement. The process in all of these sections was essentially one of muscle fiber degeneration and fibrosis accompanied by an inflammatory process" (fig 4).

Dr V. Kneeland Frantz studied the sections and reported as follows: "I could not see any evidence of tuberculosis in these sections. The lesion appeared to be a chronic inflammatory one, and I would suspect that the degeneration of muscle was a secondary inflammation. There was no evidence of tumor."

The microscopic diagnosis was chronic orbital myositis, or Zenker's waxy degeneration.

CASE 3—B. G., aged 51, a machine operator, came to the Vanderbilt Clinic in October 1940, complaining of diplopia of six weeks' duration (fig 5A).

He stated that his present illness had begun six months previously with a swelling of the left lower lid. This was not associated with redness, pain or discharge. Three months later a similar swelling appeared in the left supraorbital region. This increased slowly until the time of his visit to the clinic. He had noticed no loss of vision in either eye, no pain and no inflammation and knew of no injury to either eye. His general health had always been good, and there was no history of thyroid disease.

Examination of the eyes showed the vision to be 20/30 in the right and 20/30—2 in the left. The lids, conjunctivas and lacrimal sacs were normal. The intraocular tension was 13 mm (Schiotz) in each eye. The exophthalmometer readings were 17 mm for the right

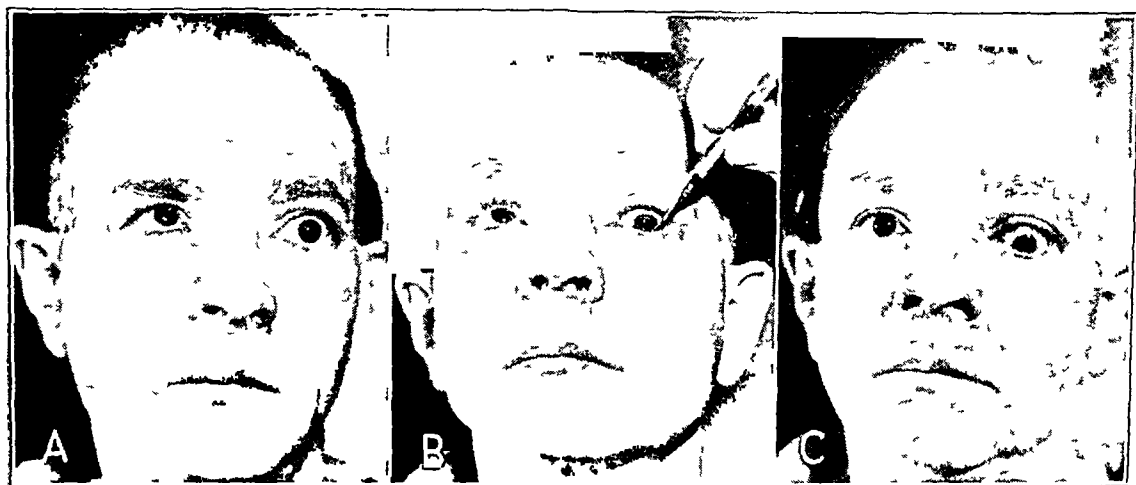


Fig 5 (case 3)—A, the patient before operation, looking up with the right eye fixing; B, a traction test, which failed to elevate the left eye; C, the patient after operation, looking straight ahead with the right eye fixing.

and 21 mm for the left eye. It was impossible to replace the left eye in the orbit by pressure backward. No lagophthalmos, no bruit and no pulsation were present. The pupillary reactions, fundi, perimetric fields and blindspots were normal. Clinical microscopy revealed nothing abnormal.

Examination of the extraocular muscles showed the movements of the right eye to be normal. The left eye was directed downward 15 to 20 prism diopters and slightly outward. The patient was unable to elevate the left eye above the horizontal plane (fig 5A).

A provisional diagnosis of intraorbital tumor associated with paralysis of the left superior rectus muscle was made and the patient sent to the hospital. While there he had a thorough clinical and laboratory study. A general physical, a urologic and a neurologic examination revealed nothing significant.

A roentgenogram of the skull, orbits and optic canals was essentially normal except that it showed some areas of porosity of the bones of the skull suggestive of parathyroid dysfunction and several areas of diminished density suggestive of metastasis. Roentgenograms of the long bones, chest, gastrointestinal tract, feet and hands did not reveal neoplasm, metastasis or sarcoid.

Because of the porosity of the bones suggestive of hyperparathyroidism, studies of the blood chemistry were made. These gave normal results except that on one occasion the protein level was 89 mg per hundred cubic centimeters, on a second examination the value was found to be 7 mg. The normal blood chemistry ruled out hyperparathyroidism.

The reaction to a tuberculin test with 1 100,000 dilution was negative after forty-eight hours, but with a 1 10,000 dilution the reaction was graded 2 plus

Since the clinical and laboratory tests did not reveal the nature of the disease, an orbital exploratory operation was recommended. Before operation two different attempts were made to elevate the globe mechanically by means of traction on a tissue forceps attached to the tendon of the inferior rectus muscle (fig 5 B). These failed to elevate the globe on two different occasions and led to a preoperative diagnosis of chronic orbital myositis of the inferior rectus muscle.

At the time of operation a lateral canthotomy was done and the wound enlarged downward to expose the orbital contents below the globe. Palpation revealed a firm mass situated below the globe and attached to the inferior oblique muscle. This extended along the floor of the orbit toward the apex and seemed to be loosely adherent to the periosteum of the floor. The mass was removed and the globe freed of its extraneous attachments. At the conclusion of the operation the globe was more freely movable with traction in all directions. The wound was closed without drainage and the patient discharged from the hospital on the fifth postoperative day.

The wound healed promptly but the left eye returned to its position of downward rotation. Ten weeks after the operation the right eye was essentially normal, while the left presented exophthalmos of 2 to 3 mm, fixation in downward rotation of about 30 degrees of arc (fig 5 C) and movement of the globe of about 10 degrees in abduction, 8 degrees in adduction and about 5 degrees in elevation and depression from its fixed position of downward gaze. The upper lid of the left eye moved freely up and down synchronously with the right when the right eye was fixing, with the left eye fixing there was a marked overaction of the levator muscle on the same side, with pronounced contralateral overaction of the right superior rectus and levator muscles. When both eyes were directed downward about 30 degrees of arc, the upper lid of each eye was at the upper part of the limbus, indicating no overaction or spasm of Muller's muscle or of the levator muscle in this position. A firm, immovable, painless, slightly nodular mass could be palpated through the lower fornix in the lower temporal quadrant in the orbit along the orbital margin between the floor and the globe. There were slight edema and fulness of the upper lid. Examinations of the exterior and interior of the eyes otherwise gave normal results.

A second exploratory operation through the external canthus and the inferior cul-de-sac exposed a firm, nodular mass of fibrous consistency wedged between the globe and the floor of the orbit in the lower temporal quadrant. This mass was dissected free from the floor and the globe. It extended backward along the inferior rectus muscle toward the apex of the orbit. An attempt was made to dissect it free from the inferior rectus muscle, but at the conclusion of the operation this muscle had been reduced to a narrow inelastic fibrous band about 6 mm wide anteriorly. A soft mass, presumably the posterior end of the enlarged inferior rectus muscle, was palpated deep in the orbit but was not removed because of its inaccessibility and because of the danger to the deeper orbital vessels and nerves. The wound was closed without drainage. At the conclusion of the operation the eye was movable in all directions of gaze.

One month later the left eye had returned to its original position of downward gaze. The patient complained bitterly of diplopia and the appearance of his left eye. A series of deep roentgen ray treatments were given without any apparent effect. With the hope of improving the patient's appearance a third operation was performed five and one-half months after the first exploration. At this time the adhesions between the globe and the floor were freed and the superior rectus muscle resected to elevate the globe to the primary position.

One year after the first operation there was no exophthalmos present, but a slight edema of the upper lid was still noticeable. The globe was fixed in the primary position, from which the patient could rotate his eye about 10 degrees to the right and to the left. Neither elevation nor depression was present, and a firm, cartilaginous mass could be palpated through the skin of the lower lid between the globe and the inferior orbital margin. Six months later the left eye once more had rotated downward about 20 degrees of arc, where it was fixed and could not be elevated or depressed. Diplopia was present, though less annoying, and the patient was gradually adjusting himself to his disability and appearance.

The laboratory report by Dr. John S. McGavic was detailed and interesting. Microscopic examination showed that the specimen consisted of muscle, nerve, fat and fibrous connective tissue (fig 6). About one half of the tissue was striated muscle, parts of this were essentially normal in appearance but a good many of the muscle fibers showed varying degrees of degenerative change. This change was characterized by pale staining, partial loss of cross striations and a granular appearance instead of the usual cleancut appearance of normal

striated muscle There was an unusually large amount of fibrous tissue, which contained relatively few nuclei and which was somewhat more refractile than usual In one place there was a localized collection of lymphocytes, but this was the only evidence of an inflammatory reaction An unusually large amount of nerve tissue was present, but the arrangement and the absence of pathologic changes in this tissue seemed to nullify its importance In summary, these sections showed only slight degenerative changes in striated muscle The changes were similar to, but less marked, than those in cases 1 and 2, in which, as in this case, a diagnosis of Zenker's waxy degeneration was made

Dr A P Stout said "This is a fragment of striated muscle which shows evidence of degenerative change, represented by fragmentation, vacuolation, loss of cross striation of the muscle fibers and some proliferation of fibrous tissue between and around the individual muscle fibers

Adjacent to the striated muscle is a rather dense mass of fibrous tissue which is peculiar in that mixed up with it are what appear to be many elastic fibers and



Fig 6 (case 3)—Lymphocytes, fibrosis and muscle fiber degeneration ($\times 200$)

what appear in the trichrome stain to be stray bundles of smooth muscle It is not a neoplasm and represents some sort of degenerative process affecting striated muscle with which I am not familiar"

Dr Fred Stewart, of the Memorial Hospital for the Treatment of Cancer and Allied Diseases, felt that this was a case of Zenker's waxy degeneration

CASE 4—J K, aged 71, a farmer, came to the Institute of Ophthalmology in November 1940, because his left eye "felt stiff and sore in the morning" In spite of the fact that he had definite limitation of upward movement and exophthalmos of the left eye, he did not complain of diplopia The present trouble had begun six months previously, after he had sprayed his trees His general health had always been good, and he gave no history of thyroid disease

Examination of the eyes showed that the vision was 20/25 in the right and 20/30 in the left without glasses The lids, conjunctivas, lacrimal sacs, intraocular tension, peripheral fields, blindspots and fundi were normal The right pupil measured 4 mm and the left 2 mm

There was slight limitation of upward movement in the left eye. The Hertel exophthalmometer gave readings of 15 and 19.

A general physical examination gave negative results. The Wassermann reaction of the blood and the sedimentation rate were normal. A routine urinalysis, red blood cell count and differential count gave normal results. An examination of the sinuses failed to reveal anything abnormal, and a roentgenogram of the head, showing the optic canals and orbits, disclosed only a slight increase in soft tissue density of the left orbit.

In five weeks the patient's exophthalmos progressed, disturbing diplopia developed and the upward excursion of the left eye became almost nil. The patient was sent to the hospital and the left orbit explored through a lateral canthotomy. The exploration revealed the presence of a large firm mass extending from the posterior surface of the globe backward along the floor to the apex of the orbit. A biopsy specimen was taken of the tumor mass and the wound closed without drainage. At the time of discharge from the hospital, five days later, the globe was once more in the primary position. One year later the patient was able to carry on his work as a farmer without complaint.

The histologic report of Dr. John S. McGavic was as follows: "The specimen consisted of muscle tissue and orbital fat. The muscle fibers when seen on long section showed loss of striation and in places had a teased out appearance. The fibers on cross section showed an incompletely filled muscle sheath and pale-staining amorphous substance instead of the usual clearcut muscle fibrillae. In places there appeared to be a proliferation of the perimysium. In several places there was a slight perivascular infiltration." The diagnosis was Zenker's waxy degeneration of the muscle.

Briefly, in these 4 cases there were the same clinical, operative and pathologic observations. Clinically there were exophthalmos, limitation of upward motility with diplopia and a positive result of the traction test. At operation in each case, the inferior rectus muscle was seen to be enlarged, firm and fibrotic and when removed cut with a gutty feeling. Histologically, in all 4 cases there were degeneration of muscle fibers, fibrosis and lymphocytic infiltration.

COMMENT

Etiology—The cause of chronic orbital myositis is unknown. Tuberculosis and syphilis have often been mentioned, even though the clinical and microscopic observations have repeatedly contradicted this claim. Some investigators have ascribed it to foci of infection, but this theory has never been proved. The fact that the inferior rectus and inferior oblique muscles are so often affected naturally tends to incriminate the antrum.

Nothing in the past histories of our patients gives a clue to the cause of the condition, for none had recently been ill. None had ever had thyroid disease, typhoid or syphilis. Sex and age may be a factor, since 3 males to 1 female is the usual sex incidence and the average age is over 40. There seems to be no relationship between the age of the patient and the severity of the condition, since some of the most rapidly developing myositis reported in the literature has occurred in patients over as well as in patients under 50. Colley²⁴ reported a case of chronic orbital myositis in a child aged 12, in which exenteration of one orbit was followed by development of the same condition in the other orbit one year later.

Briefly, there is no positive evidence that poisoning, avitaminosis, climate, heredity, diet, allergy, glandular dysfunction, infection, trauma or occupation plays any part in the causation of this condition.

Of the various etiologic theories advanced three are worthy of note, namely, the infectious theory of Offret, the lactic acid theory of Wells and the endocrine theory of Marine, Freigold, Smelzer, Aird and others.

From microscopic studies, Offret argued that the initial lesion is subacute or chronic phlebitis of the small veins or capillaries of the orbit and that all the clinical and pathologic observations of chronic orbital myositis can be explained on the basis of this conception.

In explaining the causation of Zenker's waxy degeneration in striated muscle, Wells³³ was able to show experimentally in vivo and in vitro that the histologic changes could be produced solely by an accumulation of lactic acid in the muscles. He stated the belief that some toxin produces an excessive amount of lactic acid in the muscles and that this is directly responsible for the degeneration of the muscles. Any interference with the venous circulation, such as that hypothesized by Offret, would cause an accumulation of lactic acid, thus accentuating the degenerative process.

Experimentally it has been shown that after the injection of a thyiotropic extract made from the pituitary gland the extraocular muscles of thyroidectomized guinea pigs become enlarged and present evidence of degeneration and lymphocytic infiltration similar to that noted in chronic orbital myositis. This experimental work has been accepted in some places as an explanation for the cause of so-called malignant exophthalmos associated with thyroid disease, but so far as we know it has not been advanced to explain the cause of chronic orbital myositis.

With these theories accepted as working hypotheses, it is still necessary to explain what causes the endophlebitis of Offret's theory, to demonstrate the nature and origin of the toxin of Wells' theory or to prove the presence of glandular dysfunction in chronic orbital myositis.

Gross and Microscopic Changes—At the time of operation, most observers have noted an enlargement of the extraocular muscles, sometimes to four or five times their normal size. Grossly the muscles are described as being pale, firm, smooth, friable and cartilaginous. The belly of each muscle affected usually shows a fusiform enlargement, with the ends not much affected. Sometimes the sheaths of the muscles are loosely attached to the orbital fat and the surrounding orbital tissues. One or more of the extraocular muscles may be affected, but it is a curious fact that the inferior rectus and inferior oblique muscles have been affected more often than any of the other extraocular muscles.

A number of writers have reported cases of chronic myositis affecting only the inferior rectus or the inferior oblique muscle, others have noted enlargement only of the superior rectus or superior oblique muscle. A number of observers have reported some involvement of all of the extraocular muscles. From our experience and from what we have been able to learn from the literature, it seems that any or all of the extraocular muscles may be affected but that the muscles below the globe show a special susceptibility to this disease.

Microscopically, the histologic changes were basically the same in all our cases, consisting chiefly of fibrosis, degeneration of muscle fibers and lymphocytic infiltration. Offret, who has made a special study of the histologic changes of chronic orbital myositis, tabulated the following ones as characteristic³⁴

- 1 Lymphocytic infiltration throughout the orbit with a few scattered plasma cells and a tendency to follicle formation about the capillaries. This change may be seen (a) about the central vessels of the muscle fibers, (b) in the interstitial tissue, (c) in the muscle aponeurosis and (d) in and about the individual muscle fibers.

- 2 A fibrosis between and about the muscle fibers.

33 Wells, H. G. The Pathogenesis of Waxy Degeneration of Striated Muscles (Zenker's Degeneration), *J. Exper. Med.* **11** 1, 1909, Waxy Degeneration of Diaphragm Factor in Causing Death in Pneumonia and in Other Conditions, *Arch. Path.* **4** 681 (Nov.) 1927.

34 The histologic diagnosis of chronic orbital myositis should be entrusted only to pathologists familiar with this condition, for it has been confused with a malignant process, gumma, tuberculoma, lymphoblastoma and Hodgkin's disease.

3 Marked changes in the muscle fibers themselves i. e., edema of the stroma, lymphocytic infiltration, disappearance of the striations, vacuolation, poor staining qualities, collagenous, waxy or glassy degeneration (Zenker's³⁵), changes in the nuclei, degeneration, and fibrosis

4 Vascular changes confined to the smaller veins and capillaries, which show lymphocytic infiltration in and about the vessel walls with slight endothelial proliferation but no endarteritis

Offret has studied the histologic changes characteristic of traumatic myositis, acute myositis, congenital fibrosis (Duane's syndrome, etc.) and degenerative myositis of vascular, fatty or amyloid degeneration. He maintained that these processes are different and distinct from the type of degeneration under discussion here. He stressed the point that chronic nonspecific orbital myositis must not be confused with syphilitic or tuberculous orbital myositis and cited several clinical and histologic studies of each to prove it.

Benedict³⁶ and others have stated the belief that the pathologic changes of chronic orbital myositis may vary according to the age of the process, the older processes showing more fibrosis and the more recent ones less fibrosis. Generally the orbital fat and sometimes the lacrimal gland show the same histologic picture noted in the extraocular muscles.

F. H. Verhoeft,³⁶ A. P. Stout,³⁶ Fred Stewart,³⁶ A. M. Pappenheimer,³⁶ J. S. McGavic,³⁶ Orlow¹⁸ and others have insisted that the condition is essentially one of chronic degeneration of muscle fibers, that it is not to be confused with so-called pseudotumor or granuloma of the orbit and that it is a separate and distinct histologic entity. The fact that none of our patients presented evidence of involvement of the orbital fat would be an argument in favor of this view. However, a number of cases have been reported in which chronic inflammatory changes have been noted in the orbital fat as well as in the muscles. This fact has led some writers, notably Reese,³⁶ to express the belief that chronic orbital myositis is a pseudotumor which begins in the extraocular muscles and extends from there to involve the orbital fat. It is tempting to accept the view that chronic orbital myositis is a separate disease entity, distinct clinically and pathologically from so-called granuloma of the orbit, but we prefer to await further clinical and histologic studies before becoming dogmatic on this point.

In studying the pathologic changes of chronic orbital myositis, several observers have noted the great similarity between the histologic picture of this disease and that noted in malignant exophthalmos associated with exophthalmic goiter. In fact, the histologic pictures sometimes cannot be differentiated under the microscope. At the present time there is no satisfactory explanation why these two conditions should be so similar grossly, microscopically and sometimes clinically.

Subjective Symptoms—The onset may be gradual or sudden in an otherwise healthy person. When it is gradual, there may be an interval of several months between the first symptom and the first visit to the physician. When it is sudden, this interval may be reduced to two weeks or less. In many of the cases reported

³⁵ The name Zenker's waxy degeneration has been applied to these changes in striated muscle, after the pathologist who first described this change, in the rectus abdominus muscle, in patients who had recovered from typhoid fever (MacCallum, W. G. *Text-Book of Pathology*, Philadelphia, W. B. Saunders Company, 1916, pp. 92 and 572). William Boyd (*Text-Book of Pathology*, Philadelphia, Lea & Febiger, 1938, p. 1019) stated that he had seen this change disappear spontaneously, thus giving histologic confirmation to the clinical observation that many patients may recover spontaneously if given a chance.

³⁶ Personal communications to the authors.

in the literature the onset was rather sudden and alarming, simulating the clinical appearance of an acute inflammatory process of the orbit without constitutional signs. In all of our 4 cases the onset was gradual.

The three symptoms most complained of are edema of the lids, diplopia and exophthalmos.

1 **Edema** The first symptom is usually a slight, sometimes transitory, painless edema of the lids. If this edema appears it may progress rapidly. In only 1 of our cases (case 3) did the patient notice edema of the lids before entering the hospital, and this began in the lower lid. Only one orbit was involved in each of our cases. This observation seems to be in disagreement with that of some investigators, notably Offret,¹ who stated that the second orbit becomes involved in 25 per cent of cases.

2 **Diplopia** A second, and probably the most constant, subjective symptom is binocular diplopia. Soon after the onset, all of our patients noted this symptom. Patient 1 was wearing a patch over one eye to prevent diplopia and nausea. Patient 4 did not complain of double vision, although examination showed some limitation of ocular motility in the affected eye. These findings are in complete accord with those of other writers on this subject. Therefore it seems that diplopia may be considered to be one of the most consistent and most characteristic symptoms of chronic orbital myositis.

3 **Exophthalmos** A third subjective symptom of this condition is exophthalmos. This was a fairly constant component in the triad of symptoms (edema, diplopia and exophthalmos) in our cases, being present in all but 1. In all cases the exophthalmos developed without apparent cause, and in only 1 was trauma associated with protrusion of the globe. In case 2 there was a temporary arrest, or a regression, of his exophthalmos. In some cases reported in the literature (Orlow,¹⁸ Offret¹ and others) the progress of the exophthalmos had been so sudden and so great that exposure keratitis requiring enucleation developed. In a number of cases in the literature the two orbits were affected, either simultaneously or consecutively (Offret,¹ Orlow,¹⁸ O'Brien,²² Colley,²⁴ Benedict⁴ and others) but in none of our cases were both orbits involved.

Objective Symptoms—1 **Edema** Examination of the lids in our cases gave essentially negative results except to reveal slight edema of the left lower lid in case 3. This edema was firm, painless and pale and did not pit on pressure. In none of the cases could a mass be felt in the lids or orbit.

Offret stated that most patients do not present a mass palpable through the skin. In Colley's²⁴ case, a mass could be felt through the upper lid, also, in Benedict's⁴ 2 cases a mass was noted before operation. Several other observers have noted a palpable mass before operation.

2 **Exophthalmos** The amount of exophthalmos in our cases varied from 2 to 4 mm on the Hertel exophthalmometer. Some observers have recorded an exophthalmos as high as 12 mm (Ellett) or 13 mm (Offret), but most records in the literature fail to give the exact amount present.

The displacement of the globe in our cases was either straight forward or forward and downward, with little or no lateral displacement. The exophthalmos was not reducible or affected by the position of the head. At the time of examination, it was unilateral in all of our cases. No pulsation, bruit or tenderness was present. In cases 2 and 3 measurement of the exophthalmos was difficult because of the extreme downward rotation of the affected eye.

3 Limited Ocular Motility Examination of the extraocular muscles with the eyes in the six cardinal directions of gaze revealed some limitation of ocular motility in all of our cases. Most movements of the affected eye controlled by the extraocular muscles were definitely limited. Especially was this true of elevation and upward rotation. None of our patients could rotate the affected eye upward beyond the horizontal plane. In 2 cases (2 and 3) the globe was fixed in a position of downward rotation equal to about 30 degrees of arc. In 3 a provisional clinical diagnosis of paralysis of the superior rectus muscle on the affected side had been considered. This finding, associated with exophthalmos, naturally led some clinicians to suspect a tumor behind the globe and above the optic nerve.

Most observers have noted a marked limitation of movement of the affected eye. Several have especially mentioned a weakness of elevation or a paralysis of the superior rectus muscle. Because of the frequency of limited upward motility, we believe that this finding should be stressed as perhaps the most important sign of chronic orbital myositis.

The limitation of movement in the affected eye is associated usually with strong secondary overactions of the associated muscles of the sound eye. When the affected eye is fixing and the patient directed to look slightly upward, for example, the unaffected eye shoots up under cover. Secondary overactions are noted in the other directions of gaze as well. This bizarre behavior makes it impossible to attribute the limited motility or the diplopia definitely to a paresis of any one muscle or set of muscles.

In only 1 of our cases was a partial ptosis noted. In 2 others there was a marked widening of the palpebral fissure of the affected eye when fixation and elevation of this eye were attempted. This produced a frightened, wild-eyed effect on that side.

Other Symptoms and Observations—Pain is not a characteristic symptom, although 2 of our patients complained of a feeling of fulness or stiffness about the eyes. Sometimes when pain is present it was associated with sinusitis requiring surgical intervention or with exposure keratitis. It is interesting to note that in this condition, affecting primarily the extraocular muscles, pain on movement of the globe is conspicuously absent. In acute inflammatory conditions of the orbit (abscess, tenonitis, cellulitis), pain on ocular movement is a well known and characteristic symptom.

None of our patients complained of visual impairment, except in the form of diplopia, although some observers (Benedict,⁴ Michail and Rusu,¹⁶ Ellett^{9b} and others) have reported failing vision, which sometimes develops suddenly.

Partial ptosis had been noted in 1 of our cases (case 1). Other observers (for example, Benedict⁴ and Williamson-Noble²³) have also reported ptosis. It must be stated, however, that as a general rule the function of the levator is not affected by this condition.

Perimetric field studies when done have given normal results. The pupillary reflexes, ocular media and fundi are usually normal. The fundi in all of our cases were considered normal.

Roentgen ray studies of the orbit show only a slight increase of soft tissue density. Roentgen ray studies of the gastrointestinal tract, skull or long bones have not been of diagnostic help.

According to Offret, puncture with a needle does not help in the diagnosis, and therefore we did not resort to this procedure in any of our cases. Reese, in discussing a case report by Lewis^{30w} stated that a diagnosis of chronic inflammatory

tumor had been made on the basis of aspiration biopsy. No mention was made of any change in the extraocular muscles, however.

Routine laboratory studies do not give any diagnostic help. Routine and special studies of the blood usually give values within normal limits. Occasionally a positive Wassermann reaction has been recorded in the literature, but this is unusual. The urine, sedimentation rate and basal metabolic rate have been normal. Electrocardiograms, Mantoux and Frei tests and tests for brucellosis have all given negative results.

A general physical examination usually fails to reveal anything significant. Arteriosclerosis has been reported in some cases, but this is to be expected in the age group affected. Busse and Hochheim reported a case in which the myocardium showed the same changes as the extraocular muscles. No evidence of thyroid disease was present in any of our cases.

Complications—The complications of chronic orbital myositis are chiefly mechanical. They consist principally of permanent exophthalmos, exposure keratitis, limitation of ocular motility, endophthalmitis and optic nerve atrophy.

Pathogenesis—The cardinal signs of chronic orbital myositis can be entirely explained from a study of the microscopic changes in the orbit. The edema of the lids seen clinically is due to a chronic inflammatory process affecting the orbital tissues. The exophthalmos is due chiefly to an enlargement of the extraocular muscles, with extension perhaps of this chronic inflammatory process to the neighboring tissues. The limitation of ocular motility and the inextensibility of the affected muscles are due directly to the inflammation, fibrosis and degeneration present in the extraocular muscles themselves.

Prognosis—The prognosis for spontaneous recovery is better if operation on the orbit is avoided. Some patients observed by us but not operated on have regained normal or almost normal ocular motility in from six months to a year. Those who have had biopsies of the extraocular muscles have almost without exception been worse for the surgical procedure and have sustained some degree of permanent limitation of ocular motility.

The exophthalmos usually has a tendency to regress spontaneously after the disease has run its course. Sometimes endophthalmos develops, though generally some degree of exophthalmos remains for years.

So far as sight is concerned, the prognosis is governed mostly by how much damage has occurred to the cornea from exposure. Most patients retain normal or almost normal vision, though some have become blind from extensive corneal scars. Others have suffered from optic nerve atrophy and several have lost one or both eyes from endophthalmitis.

Diagnosis—A positive diagnosis of chronic orbital myositis cannot be made without a careful microscopic study of the extraocular muscles. It is desirable, however, to make this diagnosis whenever possible without resorting to surgical intervention, since it has been shown that an operation cannot be performed with impunity. Several observers have reported an acute exacerbation of the exophthalmos with loss of the eye following a biopsy, and all are agreed that operation generally makes the condition worse. Therefore it is most essential in making the diagnosis that one keep the clinical features of the disease clearly in mind. A history of thyroid disease or of thyroidectomy makes the diagnosis much easier.

It is evident from the negative results of roentgen ray, laboratory and physical examinations of patients with chronic orbital myositis that the clinical diagnosis of this condition must depend on the diagnostic acumen of the ophthalmologist. He

must rely almost entirely on the clinical signs, the chief of which are edema of the lids, exophthalmos and diplopia. He must rule out all other orbital conditions producing this triad of symptoms, including the infectious processes of the orbit, such as periostitis, tenonitis, cellulitis, thrombosis of the cavernous sinus and actinomycosis. Also, he must exclude the noninflammatory diseases, such as malignant or benign tumor of the orbit, neoplastic disease of the hemopoietic system, mucocele, hematoma, arteriovenous aneurysm, Schüller-Christian disease with exophthalmos, metastatic lesions, paralysis of the extraocular muscles, axial myopia and certain systemic diseases (e. g., scurvy, rickets, chloroma and trichinosis).

In most of the conditions enumerated, the correct diagnosis usually presents no difficulty. In some cases of exophthalmos, however, to differentiate between some other condition and chronic orbital myositis by means of the clinical signs alone may be impossible. The number of exenterations done because of a suspected malignant process is mute testimony to this fact.

Traction Test Because of the diagnostic difficulty, we have utilized a simple test which has proved to be of some diagnostic value in differentiating the exophthalmos of chronic orbital myositis from exophthalmos due to other causes. The test consists simply of determining the passive movements of the globe in the fields of limited ocular movement. This is done by first cocaineizing the conjunctiva and episcleral tissues with 10 per cent cocaine hydrochloride (4 per cent cocaine or 0.5 per cent pontocaine hydrochloride is less effective) and then applying a fixation forceps to the tendon of the extraocular muscle in question and exerting traction in the field of limited ocular motility. For example, if there is an apparent paralysis of the superior rectus muscle with limited elevation, a wisp of cotton saturated with 10 per cent cocaine hydrochloride is placed in contact with the episcleral tissues over the tendon of the inferior rectus muscle for a few minutes. A fixation forceps is then applied to the tendon and traction exerted upward in the field of action of the superior rectus muscle. If the poor elevation of the globe is due to paresis of the superior rectus muscle, no difficulty will be encountered in elevating the globe. If, however, the inferior rectus muscle is inelastic and fibrous, as it often is in chronic orbital myositis, then the globe will remain stationary even though strong traction is exerted upward. This simple test when the result is positive therefore rules out paralysis and discloses the restrictive nature of the limitation of the ocular motility.

We found this test to give positive results in all 4 of our cases and subsequently showed histologically the presence of fibrosis of one or more of the extraocular muscles in each case.

In case 1 the test was first carried out with the patient under ether anesthesia during an exploratory operation. The patient presented moderate exophthalmos, downward displacement of the globe and clinical signs of paralysis of elevation. At the time of operation it was clearly evident that no mass was present above the globe to produce the exophthalmos and the downward rotation of the globe. A muscle hook inserted under the tendon of the inferior rectus muscle with traction upward showed that this muscle was inextensible and that the inextensibility was solely responsible for the so-called "paralysis of elevation."

In 2 other cases (2 and 3) the traction test gave positive results preoperatively. At operation in each case the inferior rectus muscle was found to be grossly inelastic, firm and fibrotic. In the fourth case the inelasticity of this muscle was demonstrated at operation.

This simple test has been helpful in differentiating clinically the limitation of ocular motility associated with chronic orbital myositis from that due to other

causes. No claim is made for its originality or infallibility, since it is obvious that it would give a positive result in a case of congenital fibrosis of the external rectus muscle (Duane's syndrome). Also, it might be misleading when traumatic or inflammatory adhesions between the extraocular muscles and the walls of the orbit were present. That such a situation can occur was demonstrated in a case of mixed tumor of the lacrimal gland seen by one of us (J. H. D.), in which the external rectus muscle was affected, producing definite limitation of ocular movement.

Having in mind the clinical picture of chronic orbital myositis and the limitations of the traction test, we would suggest the following clinical signs as characteristic of this disease: 1. Painless edema of lids with gradual or sudden onset. 2. Moderate to severe exophthalmos. 3. Limitation of ocular movement, especially upward. 4. A positive result of the traction test.

Treatment—There is no recognized form of treatment for chronic orbital myositis. Surgical intervention should be avoided if possible and if carried out should be limited to the treatment of the complications. A biopsy should not be done unless the diagnosis cannot be made in any other way. Most observers are agreed that operation on the orbit or on the muscles themselves often exaggerates the exophthalmos and generally makes a spontaneous recovery with satisfactory ocular motility impossible.

Should the integrity of the cornea become threatened by exposure, intermarginal sutures should be inserted or adhesions formed. If the conjunctiva prolapses an attempt should be made to replace it or to keep it covered with petrolatum. An evisceration or an enucleation may have to be done for complicating endophthalmitis.

Roentgen ray therapy to the orbit has been tried with indifferent results. According to Niall,^{1,2} such treatment to the pituitary gland has had no effect on this disease. This form of therapy is based on the theory that the thyrotropic hormone or some unknown secretion from an overactive pituitary gland may be the cause of the exophthalmos. Antisyphilitic treatment with the iodides and the arsenic preparations has not been of proved value, nor has it prevented extension of the disease to the opposite side. Thyroid extract has either had no effect or has exaggerated the exophthalmos. Intravenous administration of hypertonic solutions has been of questionable value. Cervical sympathectomy has been of no help.

SUMMARY

Chronic orbital myositis is a nonspecific, chronic inflammatory disease of the extraocular muscles of unknown causation. It is characterized histologically by lymphocytic infiltration, fibrosis and degeneration of muscle fibers. Grossly the muscles are enlarged, pale and cartilaginous, and they cut with a gritty feeling. Clinically the disease is characterized by (1) painless edema of the lids of gradual or sudden onset, (2) moderate to severe exophthalmos, (3) limitation of ocular movement, especially upward, and (4) inelasticity of the affected muscles as shown by the traction test described.

CONCLUSION

A positive diagnosis of chronic orbital myositis can be made only by biopsy of the affected muscles. This is to be avoided if possible, however, because of the untoward results attending surgical intervention. The correct diagnosis can generally be made from the clinical signs listed. The prognosis for spontaneous recovery is good if surgical intervention can be avoided. Treatment should be conservative and directed primarily toward preserving the integrity of the cornea.

This is best accomplished by such means as the instillation of liquid petrolatum to prevent drying of the cornea, petrolatum dressings, insertion of intermarginal sutures or formation of adhesions between the margins of the lids

Dr Ludwig von Sallmann translated much of the foreign literature listed in the footnotes

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DISCUSSION

DR JOHN S MCGAVIC (by invitation) Dr Dunnington and Dr Berke have reported a group of cases representing a distinct clinical entity not previously reported Orbital myositis has been described as a complication of thyroid disorders, as a condition secondary to adjacent inflammation (abscess, cellulitis and scleritis) in trichinosis and as an isolated histologic change not associated with any characteristic clinical picture

It has been my privilege to study the biopsy material in their cases Only two histologic entities are likely to be confused with chronic orbital myositis (1) granuloma and (2) myositis of hyperthyroidism

Birch-Hirschfeld first and later Benedict and Knight described what they chose to call pseudotumor of the orbit This term was meant to indicate how closely this lesion resembles true tumor of the orbit, many patients having had exenteration of the orbit after a diagnosis of neoplasm The lesion they described is a granuloma Unfortunately the term pseudotumor remained and has come to be thought of as the ophthalmologist's name for granuloma of the orbit

If one is to use this odd name pseudotumor, one should use it as a heading under which all non-neoplastic lesions of the orbit are placed The ophthalmic pathologist will better serve the clinician and avoid confusion in his own mind if he reports "pseudotumor granuloma," "pseudotumor hematoma," "pseudotumor myositis," "pseudotumor cyst" "pseudotumor cholesteatoma," and so on, for each of these is as much a pseudotumor as is the granuloma In fact, pseudotumor should be only a clinical term

Little will be accomplished in clearing the confusion regarding the causes of exophthalmos until the biopsy tissue already available for histologic study is classified more specifically

The first section to be shown is from granuloma of the orbit Histologically one finds tubercles made up of giant cells, some endothelial cells, lymphocytes, plasma cells and a few polymorphonuclear cells associated with a large amount of highly vascularized fibrous connective tissue The blood vessels show intimal proliferation Tuberculosis and syphilis can be differentiated readily Muscle tissue may be involved along with the orbital tissues, but there is no apparent selective affinity for muscle tissue Many such tumors have been studied at biopsy, and, although muscle tissue may be found to be involved, one does not read in the operative note that a large portion of one rectus muscle had to be removed to allow excision of the mass

Dr Berke stated that in chronic orbital myositis the muscle itself is so intimately involved that resection of the bulk of it may be necessary and in fact was in several of the cases reported

When one looks at the sections, one finds much more muscle tissue than is usual in biopsy specimens from granulomas There are focal or diffuse infiltrations of lymphocytes and plasma cells, some fibrosis and various amounts of degeneration of muscle fibers with loss of cross striations The last-mentioned change is not usual in granulomas Whether or not degeneration of muscle fibers is primary or secondary I do not know, nor has this information been forthcoming from the general pathologists It seemed to me that there should be no difficulty in distinguishing granuloma from chronic orbital myositis histologically To check my opinion, I took a group sections from what ophthalmologists call granulomas mixed

with the sections from muscles affected with myositis to a general pathologist who has done a good deal of work with muscle tissue, and he separated the sections from granulomas into a group by themselves, although he had not known that ophthalmologists have a granuloma peculiar to their specialty

After sections representing chronic orbital myositis were compared with biopsy material from patients with malignant exophthalmos associated with hyperthyroidism and hypothyroidism, it was found that there was not sufficient difference in the histopathologic changes to differentiate the two conditions. However, specimens from patients with thyroid disease showed marked variation from one muscle to another, and the material often was not adequate for proper study. It is possible that further clinical investigation will show that some of these specimens actually did not represent thyroid disease. It may be found that the cause of the two conditions is fundamentally the same, with the thyroid dysfunction a contributing factor rather than a directly causative factor even when the patient has true thyroid disturbance. At any rate in the cases reported there was more than adequate clinical evidence of the absence of thyroid disease.

Dr Dunnington and Dr Beike not only have presented a new and distinct clinical entity and described a helpful diagnostic sign, but have done ophthalmologists a service by emphasizing that they must classify the so-called pseudotumors according to their specific histologic types as far as this is possible.

DR JOHN H. DUNNINGTON. In presenting this subject we have considered the differences of opinion that may exist with regard to the entire clinical picture, but we feel that the condition is a distinct clinical entity. Some so-called cases of pseudotumor undoubtedly are instances of chronic orbital myositis, but the pathologic changes in most of these cases are very different from that found in our cases. The term pseudotumor in my opinion is a poor one and should be relegated to the scrap heap. I should like to have the pathologists more specific in their diagnoses. I believe that if they really made an effort they could subdivide the cases into their proper groups.

There are a few points which I wish to reiterate.

- 1 The apparent paralysis of elevation produced by the inelasticity of the inflamed and fibrotic inferior rectus muscle. Limitation of elevation is such a constant finding in this disease that the presence of the disease should always be suspected in a case of unilateral exophthalmos with impaired upward motility of the eye. Other conditions can produce such a mechanical interference with elevation, e. g., traumatic enophthalmos with fracture of the floor of the orbit. The traction test should always be employed to prove the cause of limited motility, and we have found it to be of great value. It is interesting that extreme traction on the inelastic muscles produces little or no discomfort.

- 2 The similarity between the pathologic changes in the affected muscles and those observed in malignant exophthalmos. This makes one wonder whether or not in some instances the two conditions have not been confused. In a few of the reported cases of malignant exophthalmos the basal metabolism was more or less normal prior to thyroidectomy, and in many diplopia was an early complaint. The frequent spontaneous recession of the exophthalmos in the two conditions is another striking similarity. Future investigation may prove that orbital myositis is the primary lesion in malignant exophthalmos and becomes aggravated by thyroidectomy. Diplopia in association with any slight exophthalmos should make one suspicious of the orbital nature of the lesion.

- 3 The prognosis is much better if operation is avoided. A biopsy is essential for accurate diagnosis but retards recovery and produces further cicatrization in the orbit.

VITAMIN E (WHEAT GERM OIL) IN THE TREATMENT OF INTERSTITIAL KERATITIS

SIMON STONE, M D

MANCHESTER, N H

Interstitial keratitis remains one of the most frequently encountered complications of late congenital syphilis. From one third to one half of patients with congenital syphilis have this disorder at some period of their lives.¹ The fact that it is most resistant to antisyphilitic therapy as compared with other lesions² has brought forth the suggestion that other factors besides spirochetal invasion of the cornea are responsible. Trauma,³ allergic states⁴ and endocrine disturbances,⁵ the last in view of the frequent onset of symptoms at puberty, have all been suggested as contributory causes. Sandler's⁶ and Arena's⁷ reports on rapid clearing of symptoms in cases of recent interstitial keratitis in from four days to three weeks after administration of sulfonamide compounds suggests that in some cases the probable cause of the acute flare-up is an organism or virus responsive to such therapy. No reports are as yet available, however, on results of this treatment in cases of long-standing interstitial keratitis. The favorable results of riboflavin therapy reported in several cases by Kruse, Sydenstricker, Sebrell and Cleckley⁸ and by Sydenstricker, Kelly and Weaver⁹ have brought forth the suggestion of dietary deficiency as a contributing cause.

The accepted method of treatment in the past consisted of at least two years of injections of compounds of arsenic and bismuth combined with large doses of iodides.¹⁰ Klauder and Vandoren¹¹ in a recent analysis of results of treatment of 532 patients found that the best results were obtained when artificial fever was

From the Neurological and Artificial Fever Therapy Services, Elliot Hospital, the Syphilis Therapy Service of the New Hampshire State Hospital and the New Hampshire State Department of Venereal Disease Control.

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9 Sydenstricker, V P, Kelly, A R, and Weaver, J W. Ariboflavinosis, with Special Reference of Ocular Manifestations, *South M J* **34** 165, 1941.

10 Levin, O L, and Behrman, H T. Treatment of Ocular Syphilis, *Arch Ophth* **23** 693 (April) 1940.

11 Klauder, J V, and Vandoren, E. Interstitial Keratitis, *Arch Ophth* **26** 408 (Sept) 1941.

combined with routine treatment. While the incidence of relapses with other methods ranged from 13 to 18 per cent, it was only 2 per cent when routine treatment was combined with fever therapy. The same authors found iodides of no value in interstitial keratitis.

PRESENT STUDY

The beneficial effect of vitamin E (wheat germ oil) on the rate of absorption of tissue exudates as observed in cases of arthritis deformans,¹² in cases of congenital nonobstructive hydrocephalus¹³ and in selected cases of pseudohypertrophic muscular dystrophy¹⁴ has prompted the use of vitamin E in the treatment of resistant interstitial keratitis. The action of the vitamin E was considered to be nonspecific, although the possibility of dietary deficiency as a contributing cause in the development of the keratitis was given consideration in view of the poor nutritional state of many of the patients. The patients treated were seen through the venereal disease control clinics of the state of New Hampshire and the syphilis therapy service of the New Hampshire State Hospital. In the past patients in the clinics with interstitial keratitis who did not respond to routine arsenic-bismuth therapy combined with oral administration of vitamin B complex were treated with artificial fever. While the fever almost always brought relief from photophobia and corneal congestion and hastened absorption of exudates of recent origin, its effect on corneal opacities of long standing was limited. The first 2 patients treated with vitamin E received artificial fever concurrently, although administration of the vitamin was begun before the artificial fever treatments were and was continued during the period of the treatments and for a number of months after they were completed. Since then, however, it has not been found necessary to administer artificial fever to any of the treatment-resistant patients in view of the improvement observed with vitamin therapy alone. Also, in 4 cases in which artificial fever treatments had been carried out months earlier for neurosyphilis and associated interstitial keratitis with little absorption of corneal opacities as a result, vitamin E therapy was started a number of months after the completion of the fever therapy, when no further improvement from the latter was expected.

PATIENTS TREATED

This study began in March 1940, when treatment of the first patient with vitamin E was begun. A total of 10 patients with advanced interstitial keratitis have been treated to date. Nine of the patients were female, and 1 was male. The oldest patient was 42 and the youngest 7 years old. The duration of the ocular symptoms was thirty-five years in the oldest patient and three months in the youngest. All of the patients had previously received one or more courses of arsenic-bismuth therapy except 1, who was treated for two years with mercury inunctions and acetarsone administered orally. One patient received intramuscular injections of foreign proteins. Two of the patients received artificial fever therapy concurrently with the vitamin therapy, and 4 received artificial fever therapy from four months to one year before having been given vitamin E for associated symptoms of

12 Stone, S. The Neurological and Endocrine Aspects of Atrophic Arthritis (Deformans), *J Nerv & Ment Dis* **97** 638 (June) 1943.

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14 Stone, S. The Treatment of Muscular Dystrophies and Allied Conditions. Preliminary Report on Use of Vitamin E (Wheat Germ Oil), *J A M A* **114** 2187 (June 1) 1940, Vitamin E in Treatment of Muscle Disturbances of Infancy and Childhood, *J Pediat* **18** 310, 1941.

involvement of the central nervous system. Four patients received vitamin E therapy but no artificial fever. Antisyphilitic therapy was administered only to patients who had not received adequate treatment in the past. None of the patients in this group received injections of arsenicals or bismuth preparations while receiving vitamin E.

All patients had severe limitation of vision in one or both eyes. Four patients had only perception of light in one eye, and 2 of the 4 had perception of fingers in the better eye with extensive dense opacities and scars over both corneas. Another patient had an opacity involving the entire cornea of one eye without perception of light in that eye but with normal vision in the other eye. She had had a partial tattooing of the involved cornea performed for cosmetic reasons. In the others the vision in the better eye varied from perception of fingers to blurring of vision. Photophobia, vascular congestion and superficial and deep corneal opacities were present in all cases.

METHOD OF TREATMENT

The vitamin E was administered at first in the form of a mixture of wheat germ oil (Lilly) with vitamin B complex¹⁵ (Lederle), 1 part of the oil to 3 parts of vitamin B complex, in doses of 8 to 12 cc daily. The vitamin B complex was added in view of its previously observed synergistic action with vitamin E. With the introduction of wheat germ oil concentrates, 50 mg mixed tocopherol capsules (Lilly) or (Winthrop) were given instead, one capsule once or twice daily, usually in combination with one or two capsules of vitamin B complex. With improvement in the patient's condition this dose was gradually reduced, so that in the end a maintenance dose of 50 to 100 mg of mixed tocopherols weekly appeared ample. Several patients received this combined vitamin therapy for twelve to eighteen months, showing gradual but continuous absorption of corneal opacities and scars. All patients except 1 who received artificial fever treatments had involvement of the central nervous system and had previously been given an average of eight to ten inductothermy fever treatments with at least two hours of fever at a temperature over 104 F at each treatment. Two began to receive vitamin E before the fever treatments were started, while with the other 4 patients the vitamin E therapy was not started till a number of months had elapsed after the fever treatments had been completed.

Three of the 4 patients who received vitamin therapy alone had received continuous antisyphilitic therapy previously for at least two years. The keratitis in 3 was of long standing, and in 2 the flare-up developed during antisyphilitic therapy. Two patients in this group received 1 to 2 mg of riboflavin three times daily for several months before vitamin E therapy was begun, without any effect on the corneal exudates, although the photophobia and the circumcorneal congestion were somewhat relieved. One patient received no antisyphilitic therapy before the vitamin therapy except oral administration of acetarsone for two years and mercury injections four years earlier.

RESULTS

The 10 patients treated can be divided into three groups: 2 with advanced keratitis who received vitamin E therapy shortly before they were given artificial fever treatments, 4 who received artificial fever therapy four to twelve months before being given vitamin E because of failure of the cornea to clear after artificial fever and 4 who received only vitamin E therapy. All showed changes for the

15 Each 4 cc of the vitamin B complex contained thiamine hydrochloride 15 mg, riboflavin 0.8 mg, nicotinamide 10 mg, pyridoxine hydrochloride 0.13 mg and pantothenic acid 0.2 mg.

better within a week after vitamin therapy was begun. Disappearance of photophobia and corneal congestion were the first changes noted. These were followed by obliteration of the capillary loops at the corneoscleral junction and wherever they invaded the cornea. The disappearance of pathologic vascularization and clearing of superficial exudates and opacities usually took place at the end of two or three weeks. The absorption of deep opacities was much slower, and in 1 of the most severely affected patients the cornea did not clear entirely for eighteen months after treatment was started.

Of the first 2 patients who received artificial fever treatments concurrently with vitamin E therapy, 1 had only perception of light in one eye and perception of fingers at a few feet in the better eye after eight months of intensive anti-syphilitic therapy, including injections of foreign protein. This patient was given vitamin therapy for a week before she was treated with artificial fever, and considerable relief from the photophobia and circumcorneal injection and some clearing of superficial opacities occurred before she received the first fever treatment. Complete disappearance of photophobia and vascular proliferation was observed after ten fever treatments, at the end of one month. The vision in the right eye was still, however, only 20/200 and that in the left eye 20/80. While the iris could be seen clearly at this time because of absorption of the superficial exudates, the fundus in the more severely affected eye could not be visualized because of residual deep opacities. Absorption of the opacities continued gradually, and six months later the vision in the better eye was 20/20, with complete disappearance of all opacities and salmon patches. The fundus of the more severely affected eye could be seen for the first time. Eighteen months after treatment was begun, complete absorption of the deep opacities and scars had taken place and the visual acuity was 20/20 in each eye. This patient continued with vitamin E in gradually decreasing doses all during this period.

A similar absorption of deep opacities took place in the second patient, although the visual impairment was less severe and the opacities less marked.

In the patients who received artificial fever therapy months before the vitamin therapy, the absorption of deep corneal opacities became apparent only after the administration of vitamin E. Again the absorption of the opacities was gradual but continuous, with a constant gain in visual acuity. One patient in this group had had her cornea partly tattooed for cosmetic reasons, as she had completely lost her vision in that eye as a result of keratitis in childhood, and return of perception of light and fingers took place after the nontattooed part of the scar had gradually become absorbed. The artificial fever was administered to this patient primarily for associated dementia paralytica. It is possible that the artificial fever administered several months earlier had played a part in initiating the absorption of the thick scar tissue.

In the patients who received vitamin therapy alone, the first evidence of improvement was manifested in disappearance of photophobia and corneal congestion, this usually within a week or ten days. In 2 patients in whom the opacities were less severe, complete clearing of the cornea took place within a month. In a patient who had had the condition for several years and had failed to respond to continuous anti-syphilitic therapy, with only perception of light in the better eye owing to deep and superficial corneal opacities and advanced vascularization of the cornea, gradual absorption of the opacities took place and after twelve months of vitamin E therapy normal vision resulted, with complete clearing of both corneas.

In the fourth patient in this group, who had only doubtful perception of light in the affected eye associated with photophobia, capillary proliferation and obscura-

tion of the iris by thick exudate, the photophobia had disappeared at the end of two weeks, with sufficient absorption of exudate so that the iris could be seen clearly. Perception of fingers at a distance of 10 feet (300 cm) returned twenty-four days after therapy was begun. The optic fundus could be seen clearly at this time. At the end of one month complete clearing of the cornea had taken place. It is significant that this patient had received no antisyphilitic therapy for at least four years before the onset of ocular symptoms and previously had received only acetarsone orally and mercury inunctions for two years. No antisyphilitic therapy had been administered to this patient since the onset of ocular symptoms, and none of the other patients in this group received antisyphilitic therapy while receiving vitamin E.

Two of the patients in this group received riboflavin in doses of 3 to 6 mg daily for several months before they were given vitamin E. As observed in patients in this group and others the effect of the riboflavin was mainly to relieve the photophobia and capillary congestion, it did not appear to hasten the absorption of corneal exudates. It is possible, however, that the riboflavin content of the vitamin B complex which these patients received—about 16 to 24 mg daily—was of some therapeutic value in relieving the photophobia and corneal congestion. The vitamin B complex was administered primarily, however, for its previously observed synergistic effect on vitamin E, and absorption of exudates continued when its use was temporarily discontinued.

REPORT OF CASES

CASE 1—I A, a 10 year old girl, was admitted to the Elliot Hospital on March 13, 1940 for treatment of resistant interstitial keratitis. The symptoms had begun about one year before admission, and although she was immediately given arsenic and bismuth therapy, no improvement resulted. Ophthalmologic examination on February 27 revealed considerable photophobia of both eyes, increased vascularization of both corneas and limitation of vision to 20/200 in the right eye and 20/100 in the left with and without glasses. On admission she showed slight notching of the teeth, prominence of the frontal bosses, photophobia, bilateral corneal opacities, nystagmoid movements of both eyes and saber shins. The vibration sense was reduced to one half over the tibias. The biceps and triceps reflexes and the knee and ankle jerks were not elicited. Examination of the spinal fluid disclosed normal pressure and dynamics, 5 lymphocytes, a total protein content of 25 mg, and a colloidal gold curve of 0¹⁰. The Hinton reaction of the blood was positive and that of the spinal fluid negative.

The patient was given wheat germ oil and vitamin B complex in a 1:6 mixture, 4 cc three times daily, and was given nine artificial fever treatments at three day intervals, with the temperature above 105 F for about two hours at each treatment. On March 26 the photophobia had disappeared, the patient was able to dispense with dark glasses and the corneal opacities were almost entirely absorbed. She was discharged on April 20 with the vision greatly improved, so that she was able to return to school.

On Feb 25, 1942 studies of the spinal fluid gave negative results, as did the Hinton test of the blood. The vision appeared good without glasses, although nystagmoid movements of both eyes persisted. Both corneas appeared clear and showed no evidence of nebulas or opacities.

CASE 2—D S, a 9 year old girl, was admitted to the Elliot Hospital on June 11, 1941, for treatment of resistant interstitial keratitis. Symptoms of visual failure in the right eye had developed gradually about a year before. As the patient failed to improve with routine antisyphilitic therapy, she was admitted to a hospital five months later for foreign protein therapy while continuing with arsenic-bismuth therapy. While she was receiving this treatment the left eye became involved.

Examination of eyes on admission showed marked photophobia, both corneas were steamy, with a ground glass appearance. The iris could not be seen, extensive vascularization of the cornea and injection of the sclera were present bilaterally, vision was limited in the right eye to perception of light and in the left eye to perception of fingers at about 2 feet (60 cm). The fundus could not be visualized in either eye. The patient was given wheat germ oil and vitamin B complex in a mixture of 1:5, 4 cc three times daily, and one capsule of mixed tocopherols daily.

On June 18 the cornea appeared less steamy and the photophobia was much less pronounced. On June 20 she was able to perceive fingers with her right eye at a distance of about 1 foot (30 cm).

On June 30, after two fever treatments and continuation of vitamin therapy, she was able to perceive fingers with the right eye and the four of spades at 12 feet (365 cm) with the left eye. On July 8 she was able to see small objects with the right eye, and the photophobia had completely disappeared. The fundus still could not be seen satisfactorily in either eye. On July 28 she had completed ten artificial fever treatments while continuing with mixed tocopherols, one capsule daily. The corneal exudate was greatly reduced, so that the iris in each eye could be clearly seen.

On August 28 the superficial exudates and opacities had disappeared entirely from the left eye and the vascular congestion and capillary proliferation had become obliterated.

On September 3 an ophthalmologic recheck showed the vision to be 20/20 in the right eye and 20/80 in the left. The right cornea showed a considerable number of interstitial opacities. There were many precipitations in the posterior surface of the left cornea. In the left eye the anterior surface of the cornea, the anterior chamber and the lens were clear. The right fundus could not be visualized, but the left could be seen clearly.

When the eyes were rechecked on November 4 the vision was 20/100 in the right, 20/50 in the left and 20/40 with glasses. The patient continued with the wheat germ oil and vitamin B complex in a mixture of 1, 3, 4 cc daily, and took 50 mg of mixed tocopherols weekly. The opacities disappeared entirely from the left eye but persisted in the right.

On March 3, 1943 the patient had 20/20 vision in each eye. All the deep exudates had disappeared from the right eye, the fundus could be clearly seen and there were no residuals except a pinpoint area at the lower part of right cornea, the remainder of a thick scar which previously had covered the entire lower part of the cornea and gradually had become absorbed. She has continued to take 50 mg of mixed tocopherols once weekly, and it is expected that the pinpoint scar will eventually disappear.

CASE 3—E. D., a woman aged 24, was seen on Aug. 27, 1940, at the Manchester, N. H., venereal disease clinic. She had had interstitial keratitis for several years, and although she had in the past received fifty-one injections of an arsenical and 107 of a bismuth preparation, the condition had progressed. When examined she showed only perception of light in the left eye, and there was complete obscuration of the left cornea by thick exudate, so that the iris could not be seen. The right cornea showed superficial and deep opacities. There was severe photophobia associated with increased vascularization. She was given 1 mg of riboflavin three times daily, vitamin B complex orally and instillations of atropine sulfate in both eyes. Except for some improvement in the photophobia and possible reduction in extent of the vascularization, the riboflavin had no effect on the corneal exudates. The patient still required dark glasses because of photophobia.

On May 2, 1941, therapy with mixed tocopherols, 50 mg daily, and vitamin B complex, one capsule daily, was begun. Two weeks later there was considerable clearing of the exudates in the left eye, and she was able to dispense with dark glasses except in bright sunlight. The dose was raised to 100 mg of mixed tocopherols daily. By August 28 the opacities had disappeared from the right eye and could be seen in the left cornea only with oblique illumination. The patient has continued to receive 100 mg of mixed tocopherols daily and one capsule of vitamin B complex. On October 27 both fundi could be seen clearly for the first time.

On Feb. 8, 1942, complete clearing of both corneas was noted. The patient has been able to return to a gainful occupation. For the last month she has been receiving wheat germ oil and vitamin B complex in a 1:5 mixture, 4 cc daily, as a maintenance dose.

CASE 4—K. W., a 14 year old girl, was seen through the venereal disease clinics of New Hampshire on Oct. 3, 1942 because of a severe relapse of interstitial keratitis of two months' duration. She had received intravenous and intramuscular therapy for two years for an attack of interstitial keratitis. The attack lasted about a year, gradually clearing after leaving many superficial and deep corneal opacities. The examination showed severe photophobia, circumcorneal congestion and capillary dilatation and bilateral corneal opacities because of which the disks could not be seen clearly. She was given wheat germ oil and vitamin B complex in a 1:3 mixture, 4 cc three times daily. In one week the photophobia had disappeared, and at the end of a month the corneal opacities had become entirely absorbed. She received no antisyphilitic therapy during this recurrence of symptoms, and the improvement resulted from the vitamin therapy alone.

COMMENT

The gradual and continuous absorption of opacities of long standing in patients with interstitial keratitis receiving vitamin E therapy, irrespective of the amount of antisyphilitic therapy they have received, suggests the possibility that other factors besides spirochetal invasion are responsible for the corneal changes. Sydenstricker and his associates⁹ have suggested dietary deficiency as an important contributing cause besides syphilis. The lack of an adequate supply of vitamins in the diet would result in a diminished resistance of epithelial membranes already weakened by syphilis against trauma, infection or the demands of puberty. Dam¹⁶ has demonstrated that deprivation of vitamin E will produce changes in capillary permeability, associated with diffuse hemorrhages and exudation of plasma, in chicks. While this would suggest that a similar causation is responsible for disturbances in capillary permeability in human beings which have in the past responded to vitamin E therapy, there is also the probability that the beneficial results from administration of the vitamin are due to the nonspecific effect of the vitamins on selected tissues in the body, irrespective of whether or not the "biochemical lesions" were caused by deprivation of vitamins. Dam¹⁶ has also reported reversal to normal in capillary permeability in vitamin E-deficient chicks after administration of lipocaine or reduction in the concentration of soluble salts in the diet while vitamin E was withheld. This nonspecific effect of other therapeutic agents in vitamin deficiency states would make it appear probable that vitamins in a like manner are capable of producing beneficial effects in certain pathologic conditions, not because of replacement of a deficiency, but because the cellular lesions in these conditions are similar to those produced by vitamin deprivation although they are of dissimilar causation. This would explain the analogous effect of vitamin E on the rate of absorption of tissue exudates in cases of interstitial keratitis and of unrelated pathologic states having increased capillary permeability as their common denominator.

Vitamin E as found in wheat germ oil and wheat germ oil concentrates, like vitamin B complex, probably contains several factors, each effective in its own sphere. Besides its effect on capillary permeability and its neurotropic and myotropic factors,¹⁷ vitamin E has been found in the past to prevent excessive proliferation of fibrous tissue in muscles¹⁸ and joints,¹² as well as in the central nervous system.¹⁹ It is probable that its administration, besides increasing the rate of absorption of corneal opacities, prevents excessive formation of scar tissue. Although the vitamin B complex was given simultaneously with the vitamin E primarily for its previously observed synergistic action with the latter,¹⁴ there is no doubt that the 16 to 24 mg of riboflavin thus received daily helped to relieve some of the photophobia and circumcorneal congestion. Its effect on the rate of absorption of corneal opacities could be discounted in view of its failure to produce such improvement when administered in conjunction with artificial fever therapy or routine treatment. Also, riboflavin when administered in doses of 3 to 6 mg daily to 2 patients several months before they had been given vitamin E

16 Dam, H., and Glavind, J. Factors Influencing Capillary Permeability in the Vitamin E Deficient Chick, *Science* **96** 235, 1942, The Effect of Vitamin E on the Blood Plasma Lipids of the Chick, *ibid* **96** 430, 1942.

17 Einarson, L., and Ringsted, A. Effect of Chronic Vitamin E Deficiency on the Nervous System and Skeletal Musculature in Adult Rats. A Neurotropic Factor in Wheat Germ Oil, London, Oxford University Press, 1938, p. 127.

18 Steinberg, C. L. Vitamin E in Treatment of Fibrositis, *Am J M Sc* **201** 347, 1941.

19 Davison, C. Effect of Vitamin E Therapy on the Central Nervous System in Amyotrophic Lateral Sclerosis, *J Nerv & Ment Dis* **97** 214, 1943.

failed to produce any perceptible absorption of corneal opacities. The accompanying photophobia and vascular proliferation were definitely improved, however. For this reason it would be advantageous to administer riboflavin in larger doses than the amount these patients received in the vitamin B complex given with the vitamin E. Johnson and Eckardt²⁰ have suggested that the capillary proliferation from the limbus into the cornea as observed in various forms of keratitis is the result of an attempt by the organism to overcome local asphyxia in the avascular tissues of the cornea by making additional oxygen available for the cells of the cornea. Riboflavin, according to these authors, through its chemical effect makes improved oxidation of the corneal cells possible, and as a result excessive vascularization becomes unnecessary. Vitamin E was observed to produce similar results by reducing excessive capillary proliferation and also caused gradual obliteration of these capillaries. The exact mechanism involved remains unknown, however.

Besides the improvement in the condition of their eyes, all the patients treated showed a notable change for the better in their physical status while receiving vitamin E and vitamin B complex. A similar favorable response has been observed in patients with *tabes dorsalis*²¹ and other forms of neurosyphilis²². This would suggest the possibility that patients with latent syphilis would benefit from an increased intake of vitamin E and vitamin B complex irrespective of the amount of antisyphilitic therapy they had received.

That concurrent antisyphilitic therapy is not always needed to produce improvement in interstitial keratitis is evident from the fact that 3 patients received no antisyphilitic treatment while undergoing combined vitamin therapy. One patient had had no treatment for four years before the keratitis developed and her previous treatment had consisted of oral administration of acetarsone alternating with mercury injections. She received no antisyphilitic therapy during the time she received the vitamin E, and clearing of the cornea resulted after four weeks of therapy with vitamin E and vitamin B complex. Her total vitamin intake during this period consisted of 900 mg of mixed tocopherols, 30 cc of wheat germ oil and 180 cc of vitamin B complex, with a total intake of 35 mg of riboflavin. This would tend to support a view entertained by some physicians that antisyphilitic therapy possibly plays a minor part in the cure of interstitial keratitis although it is of much value in preventing relapses and minimizing some of the after-effects. The safest procedure would be, therefore, to combine administration of vitamin E and vitamin B complex with antisyphilitic therapy if the patient is considered to have received inadequate treatment in the past and to continue with the vitamin therapy till all opacities have disappeared, with the dose gaged according to the patient's needs. If needed, artificial fever therapy should be used in conjunction with administration of the vitamins and chemotherapy in the treatment of patients with resistant keratitis.

SUMMARY AND CONCLUSIONS

Ten patients with interstitial keratitis were treated with vitamin E (wheat germ oil and wheat germ oil concentrate). All had received ample antisyphilitic therapy in the past. Four had received artificial fever therapy a number of months earlier because of associated involvement of the central nervous system without

20 Johnson, L. V., and Eckardt, R. E. Rosacea Keratitis and Conditions with Vascularization of Cornea Treated with Riboflavin, *Arch. Ophth.* **23**: 899 (May) 1940.

21 Stone, S. Vitamin B and E Therapy in *Tabes Dorsalis*, *J. Nerv. & Ment. Dis.*, **95**: 156, 1942.

22 Stone, S. Non-Specific Therapy of Neurosyphilis. Results from Intraspinal Administration of Thiamin Chloride Combined with Vitamin B Complex and Vitamin E (Wheat Germ Oil), *Urol. & Cutan. Rev.* **66**: 714, 1942.

its markedly affecting the course of the keratitis. Two patients were given artificial fever treatments shortly after therapy with vitamin E was begun.

Vitamin E was mainly effective in hastening absorption of superficial and deep corneal exudates, it helped to relieve the associated photophobia and reduce excessive corneal vascularization and circumcorneal congestion. In cases of long-standing involvement with extensive opacities and corneal scarring, its administration for a period of months has produced a gradual and continuous clearing of the cornea with a return of normal vision. In 1 case complete clearing of the cornea occurred after eighteen months of vitamin therapy although only perception of light was present in one eye and perception of fingers in the other when therapy was begun. Absorption of corneal exudates and return of normal vision took place in another case after four weeks of vitamin therapy alone.

Riboflavin when administered alone or in combination with vitamin E was effective primarily in relieving some of the photophobia and reducing the extent of circumcorneal injection and capillary proliferation. It appeared to have no effect, however, on the rate of absorption of corneal opacities and scars.

It is suggested that vitamin E combined with vitamin B complex is a most valuable adjunct in the treatment of interstitial keratitis. It hastens the absorption of corneal exudates and opacities of long standing, it prevents further organization of scar tissues of the cornea and it reduces excessive capillary permeability. The addition of riboflavin to the vitamin E is believed to enhance the action of the former by its beneficial effect on cellular oxidative processes in the cornea. If the patient has received ample treatment in the past, antisyphilitic therapy is apparently not needed to produce complete disappearance of the visual symptoms and corneal opacities of interstitial keratitis. Artificial fever therapy is of value mainly in preventing relapses and in producing more rapid amelioration of acute symptoms. It has little effect when administered alone on the rate of absorption of corneal opacities of long standing.

NOTE—Since this paper has been submitted for publication a second male patient with severe bilateral interstitial keratitis in a state of relapse has been placed under vitamin E and B therapy while chemotherapy is being temporarily withheld. This patient failed to show any improvement under sulfathiazole therapy and following intravenous injections of riboflavin, 5 mg daily. The clearing of the corneas has been slower in this case than in the female patients similarly treated, although the rate of improvement has been slightly more rapid than during the previous attack, when he received chemotherapy and local therapy.

Dr Walter B. Rahmanop, ophthalmologist at the Elliot Hospital, aided in the visual check-up and follow-up examinations of 4 patients. Eli Lilly and Company, through Dr C. G. Weigand, supplied some of the wheat germ oil and mixed tocopherol capsules used in this investigation. Mixed tocopherol capsules were also supplied by the Winthrop Chemical Company, Inc., and the vitamin B complex was made available by Dr J. M. Rueggsegger, of the Lederle Laboratories, Inc.

PATHOLOGIC ANATOMY OF MYOPIC EYE WITH REGARD TO NEWER THEORIES OF ETIOLOGY AND PATHOGENESIS OF MYOPIA

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Although the pioneer work of Steiger¹ has considerably enlarged the present conception of the development of the different types of refractions of the eye, there remain a number of problems in this field awaiting solution. It seems that starting from infantile hyperopia the development of the eye follows a plan of which the aim is to reach a state of approximate emmetropia. A definite correlation of growth between the various parts of the bulbus is necessary in order to accomplish this aim. Eyes with high refracting power develop a short axis, and eyes with low refraction develop a longer axis (Wibaut,² Straub,³ Wessely⁴). Thus emmetropia does not depend either on an axis of a certain length or on a certain power of the refracting system but is the result of an adequate correlation of the two. This becomes obvious when one takes into consideration the fact that the average length of the emmetropic eye varies from 22 to 25 mm (Wessely). Besides emmetropia there exists ametropia on both sides, with hyperopia on one and myopia on the other, which must not be considered pathologic but a result of normal variability. It has been demonstrated that if one draws a curve to show the number of instances of emmetropia or any degree of ametropia found among a certain number of cases, the peak is at 0.50 D of hyperopia. This means that the greatest number of persons are nearly emmetropic. Nevertheless, there is a definite difference between the shape of the curve based on statistics and the binominal type of curve which would be expected if all ametropia were merely the result of biologic variability.

In the sector of the curve covering higher grades of myopia the broadening is particularly impressive. It can be shown that the curve becomes fairly regular when one does not take into consideration cases in which there is more than 6 D of myopia (Tron⁵) or all of those in which there are alterations in the fundus, for instance conus (Betsch⁶). But even if one does not take into consideration extreme variations the curve appears too long, or, in other words, there are many more cases around the optimum ($+0.50$ D) than would be expected from purely mathematical calculations. It is not possible to answer by scientific methods the

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5 Tron, E. Variationsstatistische Untersuchungen über Refraktion, Arch f Ophth **122** 1, 1929

6 Betsch, A. Ueber die menschliche Refraktionskurve, Klin Monatsbl f Augenh **82** 365, 1929

question of why there are so many more cases of normal refraction than would be expected from calculations. One is facing here one of the mysteries of creation.

It is a fairly well established assumption that in each person the refraction of the eye is determined to a large extent by hereditary factors (Waardenburg⁷).

Having taken into consideration these facts, one might establish the limit of physiologic variations at about 6 D of myopia. Higher grades, especially when accompanied with destructive alterations in the fundus, ought to be considered pathologic with correlation having been lacking in the development of the various parts of the bulbus.

The present study involves a consideration of these grades of high myopia.

It is known that the length of the axis is the most important factor in determining the grade of such myopia. But it has been found by Schnabel and Herrnheiser⁸ that in myopia of 2 to 8 D the length of the axis varies between 23 and 26 mm, the range for emmetropia being 22 to 25 mm. In the high grades, however, the length varies from 27 to 36 mm (Wessely⁴). For this reason such grades have always been called axis myopia. This spectacular fact of lengthening of the axis led to the assumption of a stretching process which produced both the length of the eye and the alterations observed ophthalmoscopically and histologically in the fundus. Some anatomic findings, for instance the thinning of the sclera at the posterior pole, supported this theory, and once the idea was started all other alterations found in the myopic fundus were attributed to this stretching factor. Although this theory has become an almost universally accepted basis for all explanations of myopia, one must acknowledge that the existence of such a stretching factor has never been demonstrated. However, it has been claimed that the stretching is dependent on the intraocular tension.⁹

The intraocular tension is by no means elevated in the myopia in comparison with the emmetropic eye but has, on the contrary, been found reduced in about 25 per cent of cases of myopia of the higher grades (Wolff¹⁰). To meet this objection the theory was proposed that there might be a weakness of the sclera toward normal or even subnormal intraocular pressure. A statement made by Lange¹¹ pointing in the same direction, according to which the sclera of myopic eyes should contain fewer elastic fibers than the normal sclera, has been entirely refuted by Birch-Hirschfeld's¹² findings. Kuschel¹³ went so far as to claim a relation between flatfoot and myopia as a sign of weakness of all supporting tissues. However, such weakening of the sclera would probably lead to a general enlargement, or buphthalmos. Since buphthalmos develops only during the period of general growth, this theory leaves unexplained the late development of or increase in myopia. It is known, moreover, that growth of the bulbus is generally complete at about the age of 15, an age at which the myopic process not only is active but may be accentuated.

7 Waardenburg, P. J. Refraction und Zwillingsforschung, *Klin Monatsbl f Augenh* 84 593, 1930.

8 Schnabel, J. and Herrnheiser, I. Ueber Staphyloma posticum, Konus und Myopie *Ztschr f Heilk* 103 288, 1930, cited by Wessely⁴.

9 Grunert, K. Die Dehnsucht des Auges (Myopie) und ihre Behandlung, Munich, J. F. Lehmanns Verlag, 1934.

10 Wolff, E. Pathology of the Eye, Philadelphia, P. Blakiston's Son & Co., 1935.

11 Lange, O. Zur Frage nach dem Wesen der progressiven Myopie, *Arch f Ophth* 60 118, 1905.

12 Birch-Hirschfeld, A. Zur Frage der elastischen Fasern in der Sclera hochgradig kurzsichtiger Augen, *Arch f Ophth* 60 552, 1905.

13 Kuschel, J. Die Erschlaffung der Koerperkonstitution als Veranlagung zur Kurzsichtigkeit, *Ztschr f Augenh* 51 339, 1923.

So the theory was evolved that the weakness of the sclera is confined to the posterior pole and that the other layers, the choroid and retina, follow the enlargement there and become stretched. But Vogt¹⁴ previously pointed out that the alterations in the choroid and in the retina do not occur when this so-called stretching is supposed to happen, that is, when the myopic bulbus becomes oblong, but sometimes many years later. He therefore opposed this purely mechanical hypothesis and tried to find an explanation with a biologic basis. He took as his major premise the fact known in embryology that the principal part of an organ always determines its size and shape and that the surrounding protective tissues accommodate themselves to that shape, just as the size of the brain determines the size of the skull. So the retina, which undoubtedly may be considered the predominant functioning element of the optic apparatus and is indeed but an outpost of the brain, may determine the size of the bulbus. A retina with much inherent growing power, therefore, would predetermine a long eyeball and produce myopia, while a retina with less growing power might cause the bulbus to be small, with emmetropia or hyperopia. There are facts which seem to prove a relation between the size of the eye and the development of the brain. I¹⁵ have found that hyperopia is more likely to be found in children with poor intelligence. On the other hand, Braun¹⁶ saw higher efficiency in myopic than in average children. Furthermore, the eye increases from one to three and four-tenths times from birth to maturity (the brain from one to three and seven-tenths) whereas the figures for the entire body are only one to one and seven-tenths according to Wessely.⁴ I am studying the problem along this line also, but the aim of the present study is to deal exclusively with the pathologic anatomy of myopia.

I shall try to explain the pathologic anatomy in the myopic eye without relying on the stretching theory. I also shall try to ascertain whether the growing power of the retina is the determining factor in the pathogenesis of myopia or whether other possibilities must be taken into consideration.

It may be useful to begin with a recapitulation of the most important anatomic changes which are generally considered to be characteristic of myopia. They are

- 1 Lengthening of the axis of the bulbus, enlarging of the posterior part of the bulbus and thinning of the sclera in the posterior segment accompanied by a lamellar arrangement of the scleral fibers

- 2 Anomalies at the optic disk such as an oblique entrance of the optic nerve into the globe, myopic crescent, supertraction of the nerve fibers on the nasal side, temporal loop of the nerve fibers and lacunal atrophy of the optic nerve

- 3 Atrophy of the choroid and changes in the ciliary muscles

- 4 Changes in the retina, such as atrophy of the pigment epithelium, rods and cones, cystic degeneration, and total atrophy

The chronologic appearance of these changes is interesting and is of special importance in relation to the retina, as shall be seen in the discussion of the various theories. In the discussion of Vogt's¹⁴ paper, there emerged the suggestion that it would be most valuable to examine eyes in the early stages of myopia in order to find out where the first changes can be seen, as later on, when the choroid

14 Vogt, A. Zur Genese der sphaerischen Refractionen, Ber u d Versamml d deutsch ophth Gesellsch, 1922, p 68

15 Stocker, F. Ueber Beziehungen zwischen Refraction und Gehirnentwicklung (Ein Beitrag zum Refraktionsproblem), Arch f Ophth **133** 131, 1934

16 Braun, E. Beitrag zur Frage von den Beziehungen der Refraktion der Augen zur Gehirnausbildung, Schweiz med Wchnschr **65** 1124, 1935

has become atrophic, the retina of course suffers the external layers of the retina being nourished by the choroid. It is obvious that eyes in the early stages of myopia are difficult to get for anatomic examination.

While examining microscopically a great number of myopic eyes from the collection of the Institute of Ophthalmology of the Presbyterian Hospital and some from the New York Eye and Ear Infirmary, I had a chance to study histologically a myopic eye from a 15 year old boy whose second eye showed myopia of 2.75 D with typical myopic changes in the fundus. The eye had been enucleated because of severe blunt trauma with intraocular hemorrhage but without rupture of the bulbus.

The bulbus was much elongated, especially in the posterior segment, and differed decidedly in shape from a bulbus with buphthalmos due to rise of tension during growth. The accompanying table shows the measurements of this eye in comparison with a normal eye of the same age from the collection and with the average emmetropic and myopic eye according to Wessely.⁴

The following statement seems justified after a comparison of the figures in this table.

The axis of the eye of the young myopic patient was markedly longer than that of the average emmetropic eye and of the eye of a normal 15 year old boy. Furthermore, its sclera at the posterior pole appeared to be thinner than in the average emmetropic eye. Near the ora serrata the sclera was about as thick as it is in the average emmetropic eye and somewhat thicker than in the average myopic eye and the eye of a normal 15 year old boy. These

Comparative Measurements of a Myopic Eye from a 15 Year Old Boy

	Length of Axis, Mm	Thickness of Sclera, Mm		
		Posterior Pole	Equator	Ora Serrata
Emmetropic eyes (average according to Wessely)	22.24	0.06	0.42	0.53
Myopic eyes (average according to Wessely)	27.35	0.21	0.32	0.48
Normal eye from 15 year old boy	22	0.41	0.30	0.34
Myopic eye from 15 year old boy	28	0.24	0.41	0.46

findings lead to the conclusion that an enlargement of the bulbus had taken place, with the abnormal growth in length confined to the posterior segment. This is to be considered typical of myopia, in contradistinction to buphthalmos, in which the enlargement is uniform throughout the bulbus.

Microscopic analysis revealed, besides signs of intraocular hemorrhage and a slight cupping of the optic nerve, the following alterations typical of myopia.

1 Sclera. The structure of the sclera was little different from that in a normal specimen and did not show in any degree the flat arrangement of the fibers reported by several authors to be typical of high myopia. I myself have confirmed this arrangement in an eye with high myopia with an axis of 30 mm.

2 Optic disk. Neither the choroid nor the retina reached the temporal border of the optic disk. The sclera, temporally from the disk for a short distance, lay directly beneath the nerve fiber layer of the retina. Then, sharply defined, the almost normal choroid and retina appeared. There was no partial atrophy of the choroid, which sometimes extends farther temporally in cases of pronounced myopic cones. Nevertheless, there was no question of the presence of a beginning crescent. Because of an artificial defect in the specimen the real position of Bruch's membrane in that area was not well defined. On the nasal side the retina and choroid clearly overlapped the border of the optic disk, the choroid going about as far as the retina. The nerve fibers turning around the edge of the retina reached the nasal side of the optic nerve and formed a loop. The picture was typical of so-called supertraction, a phenomenon which according to my reasoning would better be called super-volution, as will be explained later. The so-called temporal loop of the nerve fibers in the area of the crescent was absent (fig. 1).

3 Choroid. The choroid was normal throughout. The blood vessels were of normal size and number in all three layers. Extensive regularly distributed pigmentation was present. Bruch's membrane was nowhere interrupted. The suprachoroid area did not show any change. Not the slightest sign of atrophy could be detected.

4 Retina The retina was normal throughout The pigment epithelium and the rods and cones showed no changes No cystic degeneration (Blessig's cysts) was present There were no signs of thinning, nor did counting of the nuclei in the different layers according to Ida Mann's¹⁷ method reveal any change A section through the macula as seen in figure 2 showed the absolutely normal condition of choroid and retina in that area

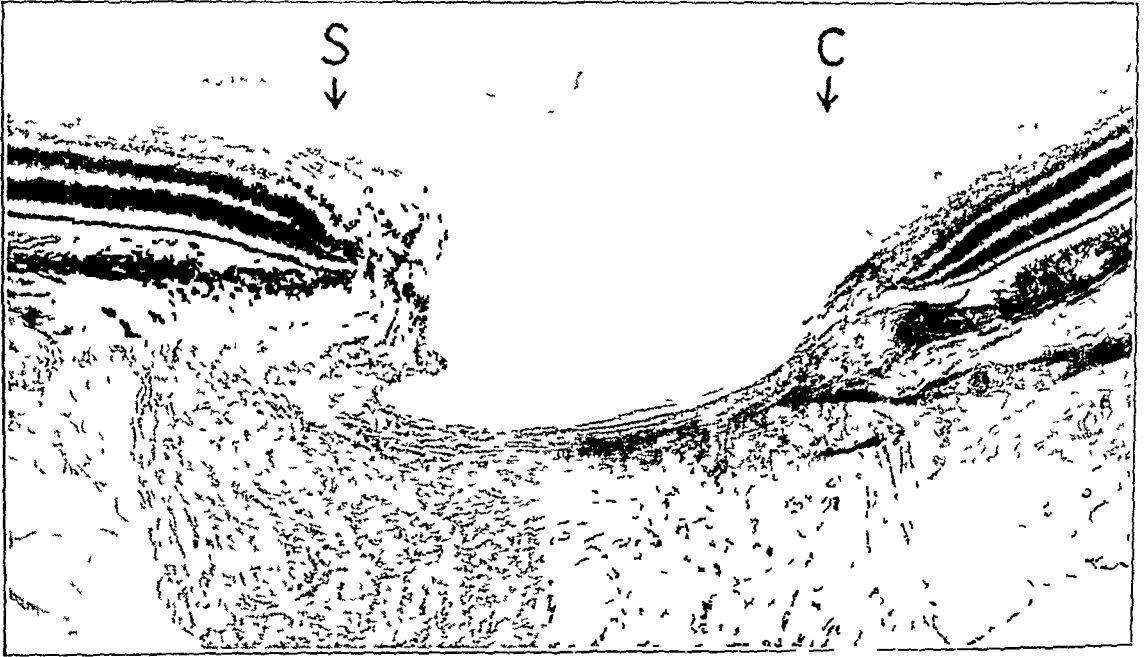


Fig 1—Optic nerve head of a 15 year old myopic patient C, crescent, S, supratraction, or supervolution

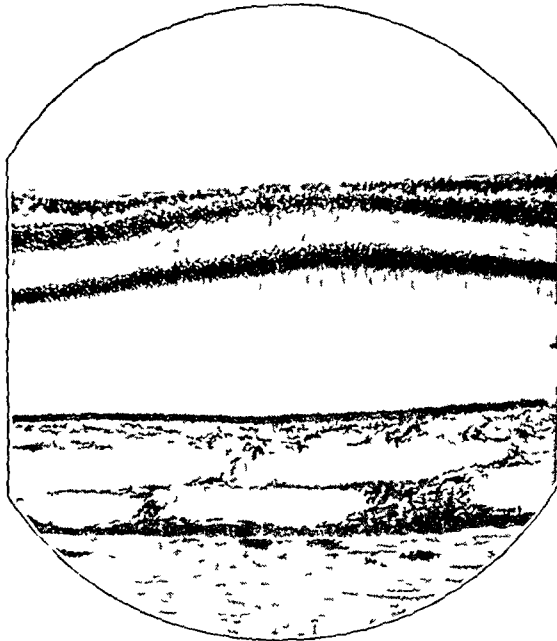


Fig 2—Region of the macula of a 15 year old myopic boy Note the perfectly normal structure of the retina and choroid

To summarize, the following anatomic changes typical of myopia were present: abnormal length of the bulbus, slight thinning of the sclera at the posterior pole, beginning temporal crescent and supertraction of the retina on the nasal side of the disk. Absent were all signs of atrophy in the choroid and the retina. It therefore may be stated that this juvenile myopic eye was already considerably larger than a normal emmetropic eye. The lengthening was accompanied by a slight thinning of the sclera at the posterior pole combined with beginning temporal crescent, no other signs of stretching being present.

I shall now leave discussion of this eye in order to review the pathologic changes in myopia in general as reported in the literature and as illustrated by my study of numerous myopic eyes. Special attention is given the question whether these changes are observed exclusively in myopia.

1 Thinning of the sclera at the posterior pole. This can be found in higher grades of myopia almost regularly and has been observed in many specimens. As the case reported reveals, it may be present at the beginning of the myopic lengthening process and therefore be considered an early sign of myopia. On the other hand, E. Fuchs¹⁸ and others have seen myopic eyes with a sclera even thicker than that in the average emmetropic eye. Extreme myopia, however, was not present among these eyes. A flat arrangement of the scleral fibers is generally found in cases of thinning. No parallel to these scleral changes has been found in senility.

2 Temporal conus, or crescent. A temporal crescent is seen frequently in high myopia both ophthalmoscopically and microscopically. But the fact that there is no inevitable relationship between the degree of myopia and the size of the crescent has been emphasized by Parsons¹⁹ and others. Although more frequent in myopic eyes, crescents are found in emmetropic and even in hyperopic eyes. The pathogenesis of the crescent, or conus, has been explained by an eversion of the sclerotic canal of the optic nerve (Stilling²⁰) and by atrophy of the choroid following stretching. Evidence for the first possibility can be seen in those cases in which repeated ophthalmoscopic examinations over a period of several years reveals the migration of a pigment spot temporally from the border of the disk as the formation of the conus progresses. Many variations can be observed in the relation between the retina and the choroid at the site of the crescent. Sometimes they remain the same distance from the disk, and sometimes the atrophy of the choroid goes much farther, being overlapped by normal retina or by retinal layers which persist in the area of the crescent. Bruch's membrane may persist well toward the disk or, conversely, may terminate well back of the retinal border (fig. 4). It is hard to say whether or not in the latter case the cause is choroidal atrophy. In this connection one should bear in mind the fact that a crescent similar to that found in myopic eyes can be seen in old eyes which are not at all myopic, as shown by Buecklers,²¹ and that the crescent is not always located on the temporal side but can be circumpapillary on the nasal or the inferior side of the optic disk. Von Szily²² found that 13.43 per cent of all crescents are not temporal ones, and he stated the belief that a tendency toward conus develops in fetal life. The pictures he reproduced from fetuses indeed resembled the ordinary crescent. It should be said, however, that conus has rarely been observed in early life, generally not appearing until the second decade. And there is no evidence that the crescent-

18 Fuchs, E. Myopische Augen mit dicker Sclera, *Klin Monatsbl f Augenh* **62** 429, 1919.

19 Parsons, J. H. The Pathology of the Eye, New York, G. P. Putnam's Son, 1909.

20 Stilling, J. Ueber den Conus, *Ztschr f Augenh* **4** 563, 1900.

21 Buecklers, M. Anatomische Untersuchungen ueber die Beziehungen zwischen der senilen und der myopischen circumpapillaeren Aderhautatrophie, *Arch f Ophth* **121** 243, 1929.

22 von Szily, A. Ueber den "Conus in heterotypischer Richtung," *Arch f Ophth* **110** 183, 1922.

like formations found in embryos would have been crescents in adults. I have a feeling that they might as well be considered transitory stages of development. Combined with the conus in many cases is the following peculiar phenomenon.

3 Temporal nerve fibers loop. In cases of crescent in which the retina overlaps the choroid toward the optic disk, the nerve fibers corresponding to the most

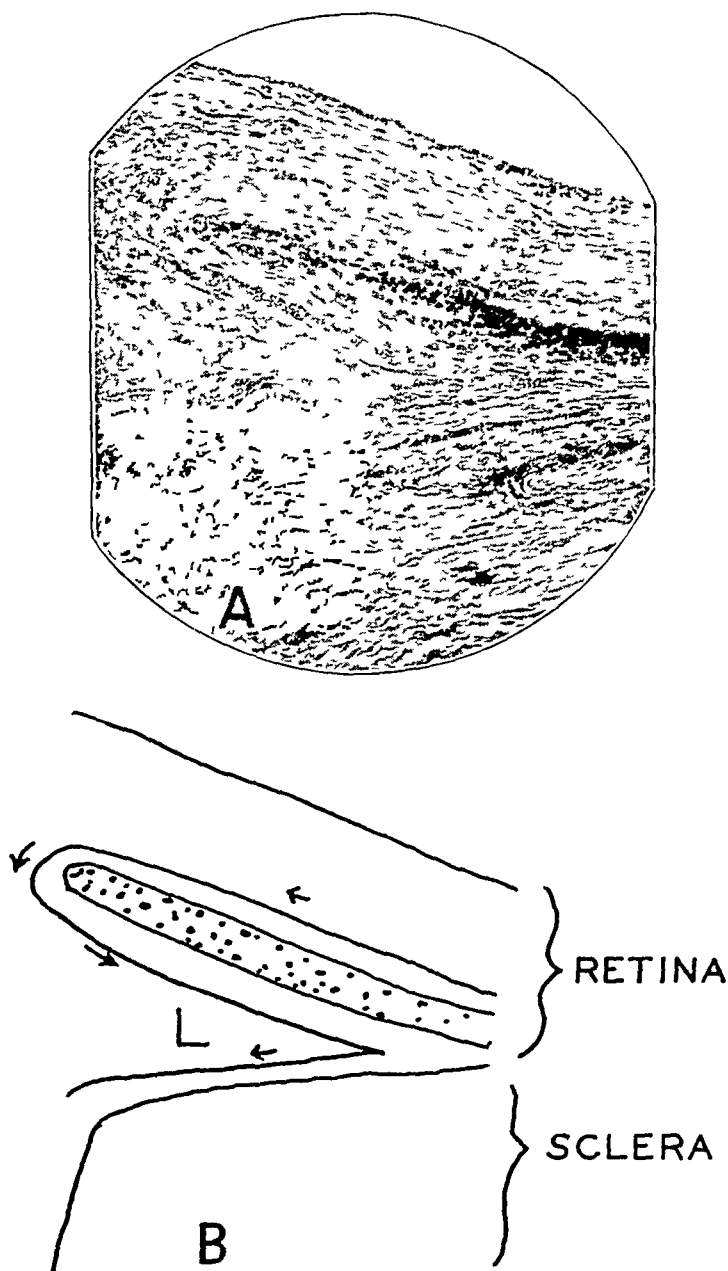


Fig 3—*A*, temporal part of the optic nerve head of a 66 year old myopic patient, with crescent and nerve fiber loop. The choroid is absent in the area reproduced. *B*, schematic explanation of *A*, *L* indicates the nerve fiber loop.

temporal part of the optic nerve happen to turn around the edge of the end of the retina, following a direct retrograde direction beneath the retina to a certain point, where they turn back in a sharp angle in order to reach the optic nerve. Figure 3, showing a section of a 66 year old myopic eye, reproduces this phenomenon photographically as far as I know for the first time, the previously published pictures

having been drawings. This anatomic peculiarity was described first by Weiss²³ and was studied extensively by Heine²⁴. The latter stated the belief that while drawn back by the stretching process Bruch's membrane by means of its ramifications extending into the optic disk pulls along some of the nerve fibers. But Siegrist²⁵ and Inoye²⁶ found that there is no evidence of such ramifications. In my investigation of Bruch's membrane I found that its site in the normal eye relative to the choroid and optic disk is subject to great variation. Sometimes it reaches far into the optic disk, going much farther than the choroid. Sometimes it stops at the border of the disk, together with the choroid. The fact that the nerve fiber loop sometimes does not reach the end of the membrane (fig 4) is one more indication of the improbability of Heine's explanation. Siegrist²⁵ gives another explanation. He could demonstrate fibers from the connective tissues of the choroid spreading

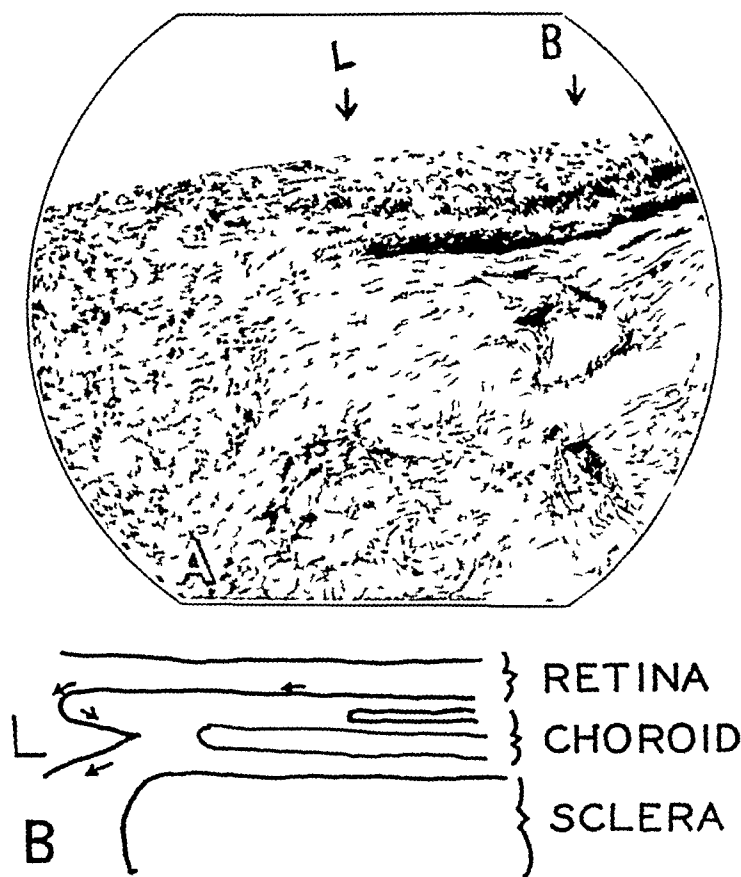


Fig 4—*A*, temporal part of the optic nerve head of a 66 year old myopic patient, *L* indicates the nerve fiber loop and *B* the termination of Bruch's membrane. *B*, schematic explanation of *A*, *L* indicates the nerve fiber loop.

out into the optic nerve head. He stated the belief that when the choroid is retracting after the stretching process these fibers may pull with it some of the nerve fibers in the neighborhood. As will be seen later, the course of the neuroglia fibers of the retina shown with Masson's trichrome stain (hematoxylin, fuchsin and aniline blue) leads me to an explanation which appears more natural. I

23 Weiss, L. Zur Anatomie der Eintrittsstelle des Sehnerven, *Period. internat. Ophth.-Cong. Ber.* 7: 339, 1888.

24 Heine, L. Beiträge zur Anatomie des myopischen Auges, *Arch. f. Augenh.* 38: 277, 1899.

25 Siegrist, A. Refraktion und Akkommodation des menschlichen Auges, Berlin, Julius Springer, 1925.

26 Inoye, S. Ueber die sog. Auffaserung der Membrana elastica chorioideae im Sehnervenkopf und ihre Rolle bei der myopen Konusbildung, *Klin. Monatsbl. f. Augenh.* 74: 124, 1925.

wish to emphasize, however, that I observed the nerve fiber loop also in an eye with senile crescent which did not show any signs of myopia. Previously Wessely⁴ pointed out that it may occur in nonmyopic eyes.

4. Supertraction of the retina over the nasal part of the disk. Often in high myopia the retina overlaps the nasal part of the disk. As demonstrated by the 15 year old eye described, it can occur in an early stage. In this eye the choroid also took part in the overlapping. This of course is not the rule. Often the choroid stops at the border of the disk and the retina alone extends farther, as shown in figure 5. Therefore the explanation given by A. Fuchs²⁷ seems not to be accurate. He said

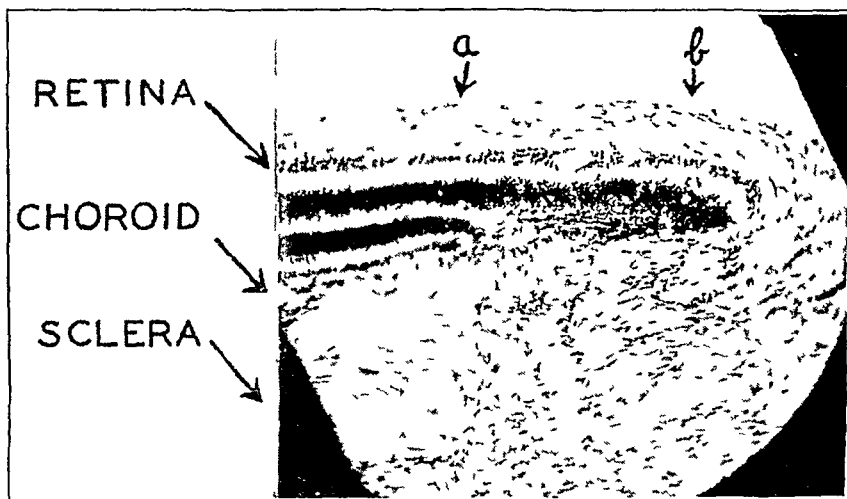


Fig. 5—Nasal part of the optic nerve head of a myopic eye, showing supertraction, or supervolution. The choroid stops at the margin of the optic disk (a), while the retina partly overlaps the nerve head (b).

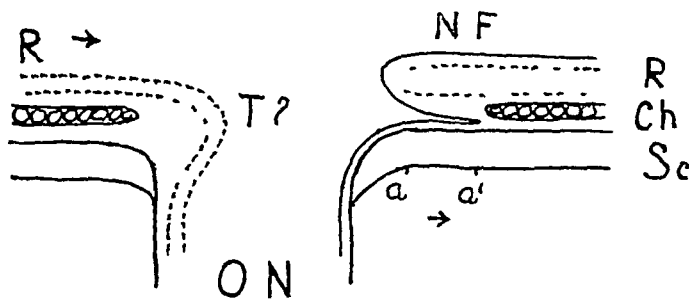


Fig. 6—Myopic crescent, nerve fiber loop and supertraction shown schematically. R, retina, Ch, choroid, Sc, sclera, ON, optic nerve, NF, nerve fiber loop, T, point where hypothetical power would have to exercise traction to produce supertraction, aa', area of crescent where the sclera is not covered by the choroid.

In cases of progressive myopia the membranes of the eye are distended more and more at the posterior pole of the eye, the distention of the sclera being greater than that of the choroid. Consequently the opening in the choroid through which the optic nerve passes is displaced temporally to the opening in the sclera so as to pull the choroid over the nasal margin of the scleral canal.

To explain this mechanical problem I drew a little sketch (fig. 6). It shows schematically the relative position of the optic nerve, choroid and retina in case of supertraction in which the choroid is not involved in the process. It is obvious

that the force of the traction should apply to point T, but it is hard to imagine what pulling power would act and how it could act there. I therefore prefer the purely descriptive expression "superposition," which implies nothing relative to the supposed mechanism (Wessely¹). I shall, however, describe later another tentative theory which would rather lead to the expression "supervolution." Although the phenomenon of the superposition is apparently found rarely in conditions other than myopia, it is not absolutely confined to myopia. Verhoeff²⁸ observed it in a case of amaurotic idiocy in which myopia was certainly absent. But this combination, on the other hand, seems not to be characteristic either. In 2 cases of amaurotic idiocy represented in the collection of the Institute of Ophthalmology of the Presbyterian Hospital I could not find it.

5 Atrophy of the choroid. It cannot be the purpose of this study to enumerate all details of the choroidal atrophy associated with myopia. One must keep in mind the fact that in the juvenile myopic eye the choroid may be without any signs of atrophy although the eye has grown considerably in length. This statement is supported by the anatomic picture in the case reported. Vogt²⁹ was certainly right when he pointed out that the atrophy of the choroid does not occur at the time of the lengthening of the bulbus but often many years later. It also must be noted that there can be a great resemblance between some choroidal changes found in myopic eyes and senile degeneration. No anatomic observations have so far been published which would support Lindner's³⁰ theory that a defective suprachoroid space would deprive the sclera of protection against the hypothetic digestive action of the tissue. I carefully examined the slides of the macular region in the case reported but could not find any signs of such deficiency.

6 Retinal changes. One of the alterations often found in myopic eyes is cystic degeneration at the ora serrata. This is not, however, regularly found in myopic eyes, nor is its appearance confined to myopia. In the juvenile eye described no Blessig's cysts could be seen. These cysts seem to be present more frequently in old age, but, on the other hand, they cannot be considered typically senile. In the material at hand I found them in normal eyes of patients 15, 27 and 47 years of age. Ochi³¹ has observed cystic degeneration in children under 4 years. Kalmer³² stated that Blessig's cysts are so frequently unrelated to a specific condition that they can hardly be considered pathologic.

I could not find other types of degeneration, such as disappearance of the pigment epithelium, crippling of rods and cones and, finally, atrophy of all the layers, except in cases of advanced involvement in which the respective parts of the choroid were definitely deteriorated. I never found retinal atrophy over a sound part of the choroid.

7 Lacunar atrophy of the optic nerve. This severe condition of the optic nerve stem is found in high myopia combined with extensive destruction of all the tissues of the bulbus. But it is also found in advanced stages of glaucoma, and there is some controversy about whether it can be found in simple myopia.

28 Verhoeff, F. H. Amaurotic Family Idiocy. Histological Examination of a Case in Which the Eyes Were Removed Immediately After Death, *Arch. Ophth.* **38** 107, 1909.

29 Vogt, A. Ueber Beruehrungspunkte der senilen und myopischen Bulbusdegeneration, *Klin. Monatsbl. f. Augenh.* **32** 212, 1924, footnote 14.

30 Lindner, K. Neue Gedanken ueber die Entstehung der Kurzsichtigkeit, *Klin. Monatsbl. f. Augenh.* **103** 582, 1939.

31 Ochi, S. So-Called Cystic Degeneration in the Peripheral Retina, *Am. J. Ophth.* **10** 161, 1927.

32 Kalmer, W. Haut und Sinnesorgane, in von Mollendorf, W. *Handbuch der mikroskopischen Anatomie des Menschen*, Berlin, Julius Springer, 1936.

alone or combined with glaucoma. At any rate, it cannot be considered typical of myopia.

In view of the facts regarding the pathologic anatomy of myopia derived from a careful study of the literature and from my observations, the issue of this study may now be considered.

There are two main questions. The first one concerns the pathogenesis of the supposed stretching process of the myopic eye. The second is, Is it necessary to admit something like a stretching process in order to understand the pathologic anatomic changes or can these be explained as well or better by another theory?

The important fact derived from study of a juvenile myopic eye is that the sclera can be thinned and the bulbus considered enlarged at the posterior pole while neither the choroid nor the retina shows the slightest pathologic change. This makes it hard to believe that the alterations found in the choroid and retina in older myopic eyes are the result of stretching. One would expect the stretching effect on the choroid and retina to appear when the enlargement of the bulbus occurs, whereas the choroidal and retinal atrophy begins much later, when the size of the bulbus has generally become more stable.

These facts are much easier to understand if one follows Vogt's¹⁴ theory that the retina is the determinative factor in the size of the eye. If the retina has a stronger tendency to grow than the sclera, the latter might be stretched. This

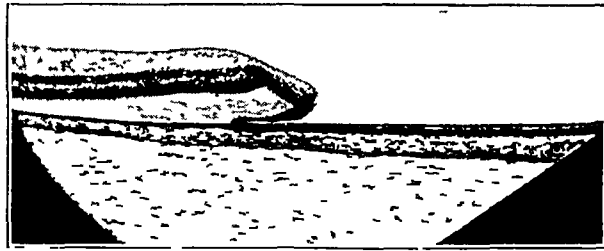


Fig. 7—Fold of retina near the ora serrata in the eye of a newborn infant

“push” of the retina on the sclera has, of course, to be taken not as mechanical but as purely biologic. Besides the fact that in a young myopic person the sclera is already affected while the retina is intact, other features of the anatomy of the myopic eye can be explained naturally by the theory. One of these is the supertraction of the retina over the nasal part of the optic disk. It should be noted that the way of postembryonic growth of the retina is not yet well known. It is the opinion of many authors that the retina does not produce new cells after birth. If there is any postembryonal growth it is to be expected at the ora serrata according to Mann¹⁷ and Kalmer.³² Whether the retinal folds I found near the ora serrata in many eyes of newborn infants have something to do with this question I do not know (fig. 7). But, although Lange,³³ who first described these folds as regularly present in the newborn, later was inclined to take them for an artefact due to fixation, the fact remains that they can never be seen in adults although the same methods of fixation are employed. One could imagine that the young tissue, still growing, in the region of the ora might be especially sensitive to the fixation chemicals and therefore give origin to these folds. If in myopia the growing retina is the determinative factor the new retinal tissue produced at the ora would push the existing retina backward. Obviously the sclera gives way

33 Lange, O. *Ber u d Versamml d ophth Gesellsch*, 1893, p. 236, *Anatomie des Auges des Neugeborenen*. Suprachoroidalraum, und sog physiologische Excavation der Sehnervpapille, *Klin Monatsbl f Augenh* 39:202, 1901.

to this biologic pressure at the posterior pole, becoming thinned, and the bulbus enlarges, whereas the retina, as the acting factor, does not show signs of stretching but follows the receding sclera. It is known that the sclera does not give way as much on the nasal side of the optic disk as it does on the temporal side. The growing retina pushes ahead over the nasal part of the disk, thus leading to the condition known as supertraction or superposition. As to the described mechanism's being more a push than a traction, I would call it rather supervolution (figs 6 and 8) depending on the inherent growing power of the retina and the choroid. The latter may take part in the overlapping or let the retina slide over. Thus it can be explained why sometimes the retina alone (fig 5) and sometimes both the retina and the choroid are present (fig 1) in the supertraction.

On the temporal side of the disk the opposite happens. There the retina finds ample space to grow because of the receding of the sclera. It may in certain cases happen that the sclera responds to the biologic pressure of the retina in an exaggerated way, so that the growing ability of the retina and choroid becomes insufficient to compensate for the enlargement of the sclera, the result being a

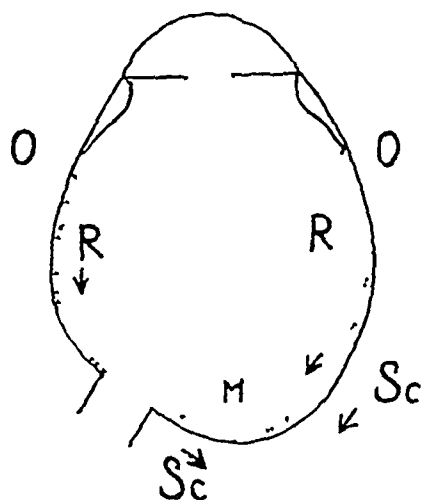


Fig 8—A drawing to show how the retina (*R*) would grow backward from the ora serrata (*O*), causing a distention of the sclera (*Sc*) at the posterior pole (*M*, macula) and overlapping of the nasal part of the optic disk—supervolution.

gap between the end of the choroid and retina and the temporal border of the disk. This will lead to the condition known as temporal crescent, or conus. The crescent therefore will be due to eversion of the scleral canal of the optic nerve on the temporal side and incongruence of growth of the choroid and retina with growth of the sclera. This may become complicated later by atrophic degeneration. If this assumption is correct the peculiar phenomenon of the temporal nerve fiber loop can be explained naturally in the following way. In figure 9, which shows a section through the optic disk of a normal bulbus, stained with Masson's trichrome stain, it can be seen clearly that at the edge of the disk a bundle of neuroglia fibers turns from the retina temporally into the inner layers of the sclera. (These fibers in reality appear red.) As the nerve fibers necessarily are interlocked with the neuroglia fibers, some of them must be drawn along with the neuroglia if eversion of the temporal side of the sclerotic canal occurs. This explanation seems to be more natural to me than a pull by choroid fibers radiating into the nerve head (Siegrist²⁵) or even by Bruch's membrane (Heine²⁴).

After a consideration and evaluation of all the facts discussed the following explanation of the pathogenesis of the myopic enlargement of the bulbus and the accompanying anatomic changes is possible:

Under the assumption that the enlargement of the bulbus is due to a stretching process it appears most likely that the determinative factor is the retina. During the initial stages of the development of myopia the retina remains normal, whereas the sclera becomes thinner at the posterior pole as the bulbus enlarges. Later atrophic changes in the choroid take place, and only after that the retinal atrophy occurs. Briefly, the pushing part naturally is not stretched, whereas the pushed sclera, having to adapt itself to the larger size of the pushing part, becomes thinner, and the arrangement of its fibers shows a change which can possibly be explained by a stretching process. The fact that the retinal vessels are often seen to be stretched out in high grade myopia does not prove a stretching of the retina proper, as embryologically the blood vessels are not of the same neuroectodermic origin. At the time when the retina begins to show atrophy there is generally no longer any considerable stretching under way. The retinal changes appear exclusively in areas where the choroid is deficient. As the choroid is supposed to supply the outer layers of the retina, its deterioration may cause damage to the latter. Thus the retinal atrophy should be considered as a secondary happening.

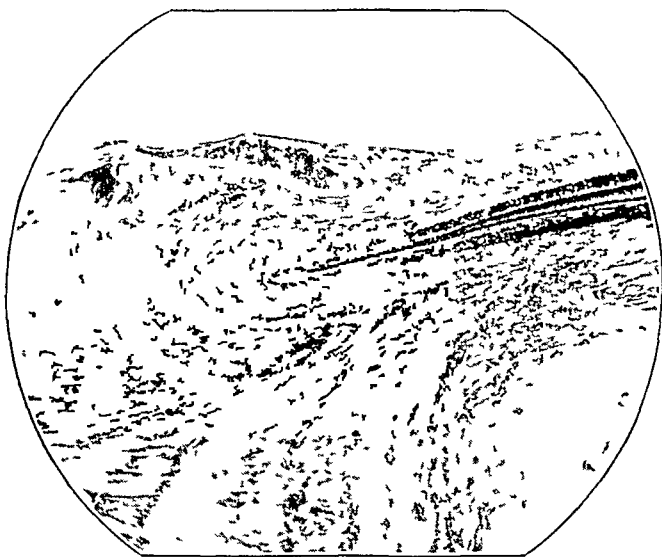


Fig 9—Temporal part of the optic nerve head of a normal eye prepared with Masson's trichrome stain. Neuroglia fibers of the nerve fiber layer of the retina turn around the end of the retina and reach the superficial layers of the sclera.

But the assumption of a stretching process is not essential to explain the pathologic anatomic changes in myopia, and the fact that the same or very similar alterations can be found in various conditions other than myopia makes it doubtful. It seems to be possible that each coat of the bulbus, retina, choroid and sclera has its own inherited potential of growth. In the majority of persons there exists enough coordination to secure the development of an eye which is emmetropic or nearly so. In myopia there would be incongruence of growth of the different constituents, not only resulting in an abnormally long bulbus but producing the various anatomic phenomena observed in myopia. An inherited degenerative factor may produce chorioretinal atrophy similar to senile changes. Most probably myopia and its anatomic attendants are not a hereditary unity but a combination of individually varying factors which may or may not result in a manifestation of myopia. This, of course, may explain the difficulty of establishing the definite course of heredity in myopia.

COMPARISON OF A NEW SENSITOMETRIC METHOD WITH USUAL TECHNIQS OF REFRACTION

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CLEVELAND

AND

LIEUTENANT COMMANDER FRANK K MOSS, USNR†

During the evolution of a new technic of subjective refraction various aspects and results have been presented¹ In the present paper comparisons are made of this sensitometric method with the usual technics of refraction from various static and dynamic viewpoints The apparatus in its present form is illustrated in figure 1 The knurled knob at the right operates the circular gradients of a specially adapted Luckiesh-Moss visibility meter, and the operator conveniently reads the settings, made by the subject, on the enclosed cylindric scale at the left The position of the convergence target is shown for a test of near vision Various details of the apparatus and technic are omitted here, as they have been presented heretofore^{1a}

SYNOPSIS OF METHOD

The sensitometric is a subjective method of refraction in which the dioptric power producing maximal visibility is determined with the Luckiesh-Moss sensitometer^{1a} The measurements of visibility are derived from brightness contrast rather than from acuity thresholds By means of a convergence target of sufficient size and indistinctness, as illustrated in figure 2, the visual thresholds are determined with binocular convergence in force but in the proved absence of any adequate optical stimulus for relative accommodation This new technic also differs from the usual subjective tests in that identical procedures are involved in both static and dynamic tests Thus the data obtained under conditions of near and of distant vision are directly comparable In a detailed laboratory study of 20 cases and a clinical study of 100 cases, the method indicated (1) that for the typical emmetropic subject, the eyes in the so-called "position of rest" are accommodated for a point anterior to the retina to the extent of about 0.75 D and (2) that for such a subject there is no evidence of a lag of accommodation within the range of habitual near vision

STATIC REFRACTION

Control of Relative Accommodation—This compensatory function is avoided in the sensitometric procedures by elimination of all adequate optical stimuli for accommodation from the entire binocular field^{1b} The attainment of this essential control is experimentally proved by symmetric relationship between visibility and

† Lieutenant Commander Moss died Feb 14, 1943

From Lighting Research Laboratory, General Electric Company

1 Luckiesh, M, and Moss, F K (a) New Method of Subjective Refraction Involving Identical Technics in Static and Dynamic Tests, Arch Ophth **23** 941 (May) 1940, (b) The Avoidance of Dynamic Accommodation Through the Use of a Brightness-Contrast Threshold, Am J Ophth **20** 469 (May) 1937, (c) The Plus-Power Bias in Static Refraction, Am J Optom **18** 313 (July) 1941, (d) Functions of Relative Accommodation, Am J Ophth **24** 423 (April) 1941, (e) A New Method of Subjective Refraction at the Near-Point, Am J Optom **18** 249 (June) 1941, (f) Initial and Residual Effects of Ophthalmic Prisms on Visibility and Accommodation, Arch Ophth **29** 968 (June) 1943

refraction about the dioptric axis of maximal visibility. In other words, over and under additions of equal dioptric powers blur the vision to equal degrees.

In the fogging method of refraction, it is probable that relative accommodation is avoided in the initial phases of the examination. However, the stimulus for relative accommodation increases in intensity as the plus power is reduced, and this function may be influential in the final stages of the fogging test. Furthermore, it is not certain that both positive and negative relative accommodations are completely avoided in these procedures, particularly when an exact correction is sought.

Control of Convergence—The sensitometric method involves binocular parafoveal stimuli of sufficient intensity to insure convergence at a point in the plane

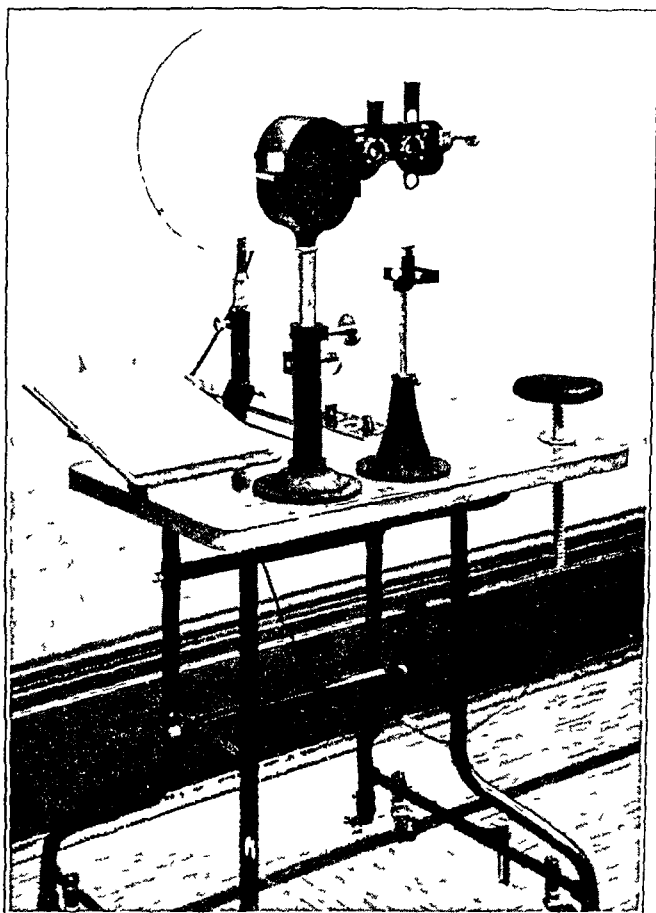


Fig. 1—The Luckiesh-Moss sensitometer in its latest form. The position of the convergence target is shown for a test of near vision.

of the test object.^{1a} The blurred luminous stimuli for convergence have been shown to be inadequate stimuli for relative accommodation. In the usual methods of examination, monocular and foveal stimuli for accommodation as well as convergence are present. It has been shown that the refractive differential between binocular and monocular control of convergence is of the order of 0.25 D in the cases which have been studied. In general, the indicated lead of accommodation is less under binocular than under monocular control. (Briefly, "lead of accommodation at the far point" may be described as the amount of negative power required to produce maximum visibility when negative relative accommodation is prevented.)

Criteria of Emmetropia—The sensitometric correction of ametropia is that which produces maximal visibility without the exercise of relative accommodation. Thus it is absolute in this respect so far as any physical constant can be so considered from a physiologic viewpoint. On the other hand, the usual static correction is that which yields an arbitrary degree of visual acuity. Thus it is empiric in this respect. In addition, the usual methods of measuring visual acuity are limited in precision. This presumably minor handicap is eliminated in the sensitometric procedures by the averaging of a sufficient number of quantitative measurements of visibility.

Dioptric Biases in Usual Subjective Tests—The usual subjective procedures are clinically biased in the direction of plus power owing to the practice of determining the maximal amount of plus power which is acceptable without an appreciable loss in visual acuity.^{1c} If it were not for this bias, the prescription

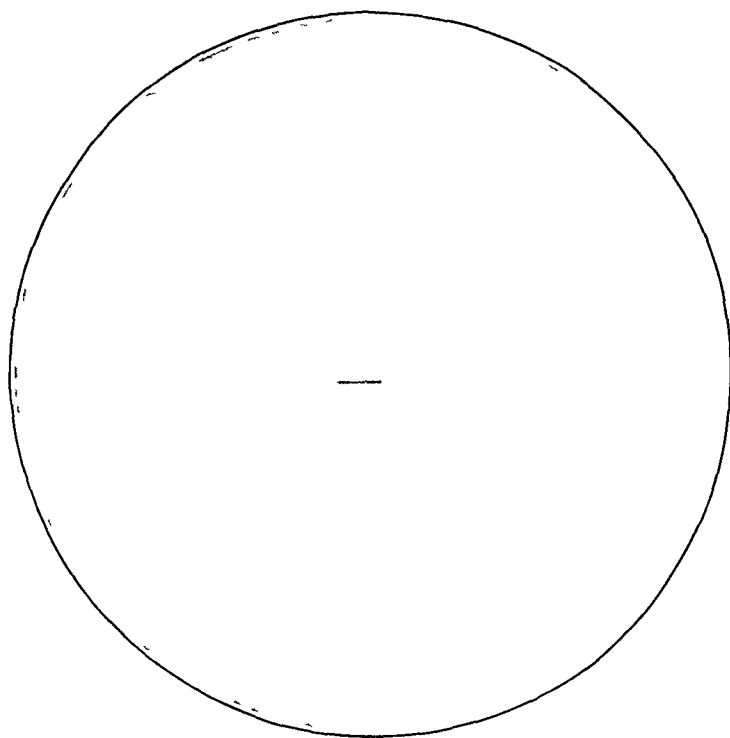


Fig. 2—The convergence target and the biconcave test object, which are crucial components of this new sensitometric technic

would be excessive in minus or deficient in plus power, and the not infrequent disparity between the usual subjective and objective methods would be greater than it is. Thus an apparent check between the usual subjective and objective tests appears to be due, in part, to empiric biases in the methods of testing. In general, it is probable that the plus power bias has been more or less indirectly introduced in static tests in order to obtain satisfactory corrections for near as well as for distant vision. If this assumption is correct, it follows that so-called static findings are not correctly designated as "distant corrections."

Negative Relative Accommodation—The existence of a plus power bias in static tests favors the generally accepted theory that the normal adult eye is incapable of negative relative accommodation at distance. A priori this conclusion necessitates assuming that the adjustment of negative relative accommodation, which is available to the extent of several diopters in near vision, is absent entirely in distant vision. If this is a characteristic of the normal eye, it appears to be an

unfavorable one from the mechanical viewpoint of efficiency in making accommodative adjustments

Ease of Seeing—The normal adult nonpresbyopic eye is found to be myopic to the average extent of about 0.75 D by the sensitometric method with binocular fixation and in the absence of relative accommodation. When the indicated myopia is corrected with lenses, prolonged and critical distant vision is found to be easier, as is revealed by a markedly lower rate of involuntary blinking.^{1a} If the eyes were actually emmetropic, rather than myopic at distance, it follows that the addition of -0.75 D would constitute a stimulus for positive relative accommodation. Hence such a dioptric addition should augment rather than lower the rate of blinking during performance of a task demanding critical vision at distance.

Teleologic Considerations—Since seeing is demanded at various distances and usually with frequent alterations in fixation, it seems improbable that the visual mechanisms would develop so that the state of ocular repose would be coincident with the extreme condition of distant vision.^{1d} On the contrary, it seems more reasonable to assume that the "state of repose" would be coincident with some compromise position between the extremes of distant and near vision, particularly from the viewpoint of mechanical efficiency in shifting from long to short range and vice versa. The latter hypothesis is supported by the accommodation-convergence relationship determined for the normal subject by the sensitometric method.

Static Definition of Emmetropia—Emmetropia is defined as "the normal state of the ocular refractive system in which infinity and the retina are conjugate with or without the exercise of relative negative accommodation." It is to be noted that although the static sensitometric examination indicates that the normal eye is myopic in the absence of stimuli for relative accommodation, it may become emmetropic when such stimuli are present. In certain cases involving prolonged, critical, distant vision it has been found advantageous to substitute negative lens power for negative relative accommodation.

DYNAMIC REFRACTION

Direct Dynamic Refraction—The refraction in near vision is measured directly by the sensitometric method.^{1e} At present this method is the only one which yields such information directly, as correction factors must be applied in other dynamic methods of refraction. Obviously such correction factors are the least appropriate in certain anomalous cases in which precise correction factors are most needed.

Control of Relative Accommodation—The avoidance of this function by the sensitometric procedures appears to be as complete in near vision as it is in distant vision. Actually, the methods are identical at these extreme fixation distances. This is not a characteristic of other subjective methods.

Lag of Accommodation—Since a blurred retinal image is assumed to constitute a stimulus for accommodation, it seems unlikely that a normal eye, capable of several diopters of relative accommodation, would remain definitely out of focus in critical near vision. If a deficiency in accommodation actually existed, its correction by relative accommodation should result in greater subjective fatigue and discomfort than appears to be experienced in prolonged near vision.

Effects of Prisms on Refraction and Visibility—Exploratory sensitometric tests indicate that base-out prisms cause emmetropic eyes to become myopic, whereas base-in prisms produce a hyperopic condition.^{1f} These refractive changes appear to

be approximately equal in magnitude at the usual reading distance. Obviously, equal and opposite refractive changes would not result if the accommodation lagged with respect to convergence. It has also been demonstrated with emmetropic subjects that base-out and base-in prisms of equal powers lower the visibility of a given test object by approximately equal amounts. Obviously, such a result would not be expected if the assumed lag of accommodation existed in reality. Tests made at a distance of 6 meters indicate that the so-called emmetropic subject obtains the highest degree of visibility with the addition (right eye) of a 4 D base-in prism. Since abduction results in a decrease in the refractive power of the eye, the attainment of maximal visibility at distance with base-in power is consistent with the static sensitometric finding of myopia with distant fixation.

Ease of Seeing—The sensitometric examination reveals that emmetropic subjects obtain maximal visibility over a wide range of near vision without the addition of dioptric power. It has also been shown that the addition of either plus or minus power before the eyes of such subjects increases the effort involved in seeing, as indicated by a marked increase in the rate of involuntary blinking during the performance of a critical near vision task.¹⁴ If the accommodation lagged behind convergence in near vision, as has been postulated, the addition of plus power should increase the visibility of objects and make seeing easier. Neither of these results is obtained with additional plus power. In fact, the addition of plus power may slightly decrease visibility and markedly increase the rate of involuntary blinking.

Clinical Tests of the Sensitometric Method—The corrections indicated directly by dynamic sensitometry have been shown to be appropriate in such diversified cases as those in which there are (a) normal or expected clinical data, (b) high dynamic retinoscopic and crossed cylinder findings, (c) low dynamic retinoscopic and crossed cylinder findings and (d) high degrees of exophoria or esophoria. Furthermore, the dynamic sensitometric corrections have been found to be satisfactory for both distant and near vision in those cases in which single ophthalmic corrections are possible.

Dynamic Definition of Emmetropia—The normal states of adult nonpresbyopic eyes in which all points within the range of habitual near vision and the retinas are conjugate without the exercise of relative accommodation (and with the static addition), while more distant points may become conjugate by the exercise of negative relative accommodation.

Nela Park

TUBEROUS SCLEROSIS

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NEW YORK

Tuberous sclerosis, a disease entity first described by Bourneville in 1880 and often given his name, cannot really be considered by itself but must be looked on as a part of a group of diseases known as the phakomatoses. This name, derived from the Greek word *φάκος* in its meaning of "birthmark," was suggested for the group because of the common characteristic of cutaneous lesions. There are now recognized in this classification four separate entities: tuberous sclerosis, or Bourneville's disease, neurofibromatosis, or von Recklinghausen's disease, angiomatosis, or von Hippel-Lindau disease, and, most recently added, the Sturge-Weber syndrome. All are characterized, as previously stated, by cutaneous lesions, which are respectively typical, and by an amazing variety of other lesions scattered throughout the body. The lesions, however, are predominantly important in the eye and make the syndromes commandingly significant to the ophthalmologist. But it is not the purpose of this paper to discourse academically on this disease group but merely to report a rather typical case of tuberous sclerosis which has recently come under my observation.

A 10 year old boy of Greek and Italian extraction was first seen in the clinic of the Manhattan Eye, Ear and Throat Hospital on March 11, 1942, having been referred by the school nurse.

The father and mother, about 36 years of age, were in good health. Both stated that their "eyes had always been good," and subsequent ophthalmoscopic examination revealed no abnormalities in the fundi of either. The patient was an only child, there had been a previous miscarriage. No history of any ocular trouble in the grandparents or other relatives could be elicited, but according to the parents a maternal uncle had died at 17 of "tumors of the heart" and the maternal grandmother had died at 61 of a "tumor on top of her heart which choked her" and which was spoken of as a "thyroma." Another maternal uncle, now in the Army, wrote that "the Army doctors had found something wrong in the back of one of his eyes."

The patient had seemed entirely normal at birth, but at 6 months he had attacks of generalized twitching and would stare straight ahead, these spells continued almost nightly. It was also noticed that he was cross-eyed. At 15 months he had a bad fall down the stairs. At 7 years he had an acute febrile illness which was diagnosed as encephalitis. He reputedly had a temperature of 107 F, was in a coma for four days and did not recognize persons for some time afterwards. The spells became less frequent after that, occurring only every ten to fifteen days, usually at night. According to the father's description of the attacks, there was rigidity as well as generalized twitchings and violent jerkings, more marked on the left side, twisting of the eyes and grinding of the teeth and usually unconsciousness.

He started school at the age of 6 years but stopped for some time after the so-called encephalitis, at the age of 7, and again for a year at the age of 9, on the advice of his teacher, supposedly because of nervousness. He had just returned to school in an open class, and his parents admitted that he did very poorly in his work and was not cooperative.

External examination revealed fairly typical adenoma sebaceum of the face, with a butterfly distribution across the bridge of the nose and cheeks (fig 1). The eyes showed a convergent, nonalternating strabismus with poor central fixation of the left eye, but the extraocular movements were well performed. The scleras were white, the pupils were entirely normal and the tension seemed normal on finger palpation.

Read before the Section of Ophthalmology, New York Academy of Medicine, Dec 21, 1942

Uncorrected vision in the right eye was 20/20 —2 and in the left eye 20/400 eccentrically. The fields were difficult to take, but there was good light projection in both eyes. A roughly charted field for the good eye showed marked generalized constriction.

The slit lamp examination gave entirely negative results. The ophthalmoscopic examination, however, disclosed a striking picture. The media were entirely clear and the fundi well seen. Figures 2 and 3 show drawings of the fundi.¹ Below the disk and adjacent to it there was a large flat whitish area, and above the disk there was a smaller, similar area in the center of which there were a few tiny cysts. Temporal to this there was a fully developed, though small, cystic swelling. This is of interest because it supports the view that the flat whitish tumors often seen in this condition are simply precursors of the more typical elevated cystic tumors. The left eye showed a much more advanced picture. There were three tremendous cystic swellings, one on the disk, and one above and one below the macula. In spite of the size of these lesions, no hemorrhages or cystic buds floating free in the vitreous, as frequently reported, were seen.

Roentgenograms of the chest and sinuses were normal, the Wassermann reaction was negative and a roentgenogram of the skull was reported to show "three or four areas of

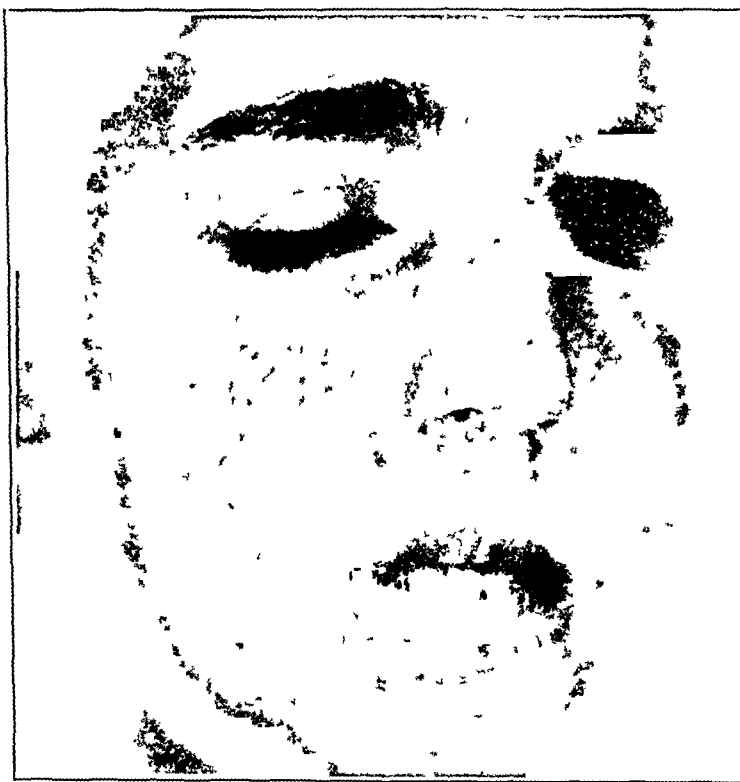


Fig 1—The patient, showing adenoma sebaceum of the face

calcification in the brain substance, probably in the choroid plexus." General physical examination revealed nothing further except some patches of vitiligo, a few pigmented lesions and several small fibromas scattered over the body.

The patient was seen by a neurosurgeon, Dr Thomas I Hoen, who had an electroencephalogram made. The record was reported abnormal and compatible with a diagnosis of tuberous sclerosis.

The patient was last seen on December 9. He had been taking phenobarbital for five months, and his father reported that there had been no convulsions except several which had accompanied an undiagnosed acute febrile illness one month previously. He was, however, having considerable difficulty in school, and the parents often found him "very hard to handle," as they expressed it. There were a new small flat whitish lesion in the lower temporal quadrant of the right fundus and a possible slight increase in size of the old lesions, but otherwise no change in the ocular condition.

1 It should be explained that a mistake was made in the drawing reproduced in figure 2, so that it appears to be the left fundus, but it is really a mirror image of the right fundus and the lesions are all correct in their relation to the disk.

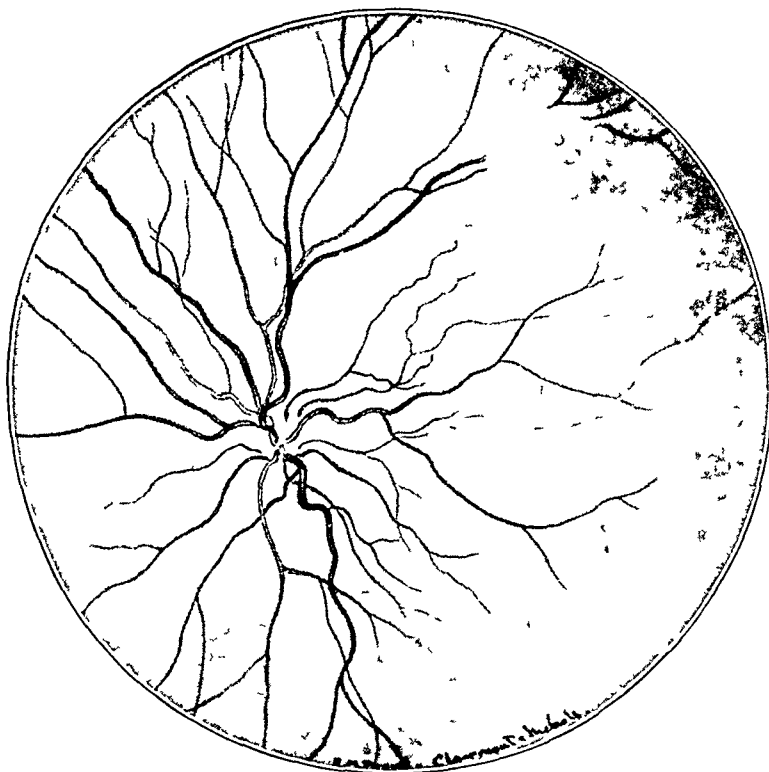


Fig 2—Drawing of the right fundus (owing to the artist's error this is a mirror image), showing flat whitish tumors and early mulberry-like tumors



Fig 3—Drawing of the left fundus, showing advanced mulberry-like tumors

This case is of interest because it presents the classic triad of Bourneville mental deficiency, epilepsy and adenoma sebaceum, and, in addition, roentgenologic and electroencephalographic changes in the brain, as well as the striking ocular lesions

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DISCUSSION

DR THOMAS I HOEN Tuberous sclerosis has been known as a clinical entity since the middle of the last century, but cases are rare and it has been difficult to follow the patients throughout the course of the disease, so that the complete pathologic picture is not so well known as the clinical picture. It is known, however, that the abnormalities seen in the retina are a part of a general neoplastic tendency on the part of the patient. Many persons have thought the condition was limited to tissues of ectodermal origin, but this is not true, as rhabdomyoma of the heart and other forms of mesodermal tumor are frequently found. However, the picture is characterized by striking changes in the fundi, the skin and the central nervous system. The changes in the central nervous system are multiple enlargements, for example of glial tissue, often considered not to be true tumors, although I believe it is fairly generally recognized now that they are true tumors of glial origin. The cells of the tumors in the fundus and in the brain are typical of the cells of tumors of the astroglia group as classified by Cushing and Bailey. They have the typical fibrillary structure, many tube-feet attached to blood vessels are seen and they frequently undergo cystic degeneration, which is also a characteristic of astrocytomas in general.

I saw the boy described by Dr Constantine, and we had an electroencephalogram made, which I shall not describe except to say that there were abnormal waves of average voltage and a slow rhythm, which are characteristic of neoplasms in general. The fact that the slow waves could be picked up over various parts of the cortex strengthened the feeling that the boy had numerous tumors in the brain. A pneumoventriculogram could have been made. The characteristic picture, instead of the pretty butterfly picture, shows irregularities and distortion of the ventricular contour. It is common to find tumors of the choroid plexus, they are waxlike nodules on the choroid called "candle drippings." The calcification in the choroid shown by the roentgenogram might have been in a tumor because such tumors often undergo calcification.

The clinical and the pathologic picture are well known, but there is no known method of treatment other than symptomatic handling. This patient had seizures, and he was known to be mentally deficient. He was given anticonvulsant drugs, which stopped the seizures, nothing could be done to improve his mental status or prevent loss of vision from the tumors in the fundi. We hope we shall be able to follow this case to its ultimate conclusion, which is not far in the future. Some authors have recommended decompressive operations in such cases, but I do not believe that they are satisfactory. If signs of intracranial hypertension are present, the decompression will prolong life somewhat, but not very happily.

In conclusion, I would say that this condition, while rare, is more common in certain places than in others. It was identified first in continental Europe and is more common there. It is rare among Anglo-Saxons, occurs in Negroes and occurs rather frequently in the Japanese.

DR HARRY McGRATH About three years ago I had the opportunity in a mental hospital of observing a case of tuberous sclerosis with the typical syndrome of adenoma sebaceum, convulsions and mental deficiency. There was a smooth white mass on and above the disk in the left eye. It was not of the mulberry type described by Dr Constantine. There was no other lesion in either fundus.

In the course of four months there was no change in the shape and size of the tumor. At the end of that time the woman suffered fracture of the skull in a

fall, and she died shortly afterward. The eye became available for microscopic study. This case, with the pathologic study, was reported in a neurologic journal but has not been mentioned, to my knowledge, in the ophthalmologic literature, although I understand it was only the second case in the United States in which a microscopic study of such a tumor was made.

Grossly the tumor was cystic. It had its origin in the nerve fiber layer and involved the rest of the retinal layers only by pressure. The cells were astrocytes with processes embracing the vessels. The pathologist who examined the sections was of the impression that it was a glial tumor of low growth possibilities and not a congenital malformation. The sections are available for study.

REOPERATIONS FOR GLAUCOMA

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NEW YORK

The return of hypertension after an apparently faultless operation for glaucoma is a *bête noire* of the ophthalmic surgeon. It cannot be predicted or forestalled. It must simply be accepted as one of the hazards of glaucoma to be dealt with as well as possible.

The literature is replete with indications and contraindications for primary operations, but there is little general agreement as to the relative efficacy and value of the operations themselves. This is undoubtedly due to a lack of understanding of the etiology and pathology of glaucoma. Each operation is designed to relieve only the hypertension, by removing the obvious barriers to filtration or by providing a vicarious pathway. The underlying disease is not cured by the removal of one of its symptoms.

In spite of innovations and modifications of operations for glaucoma, little factual or practical progress has been made within the past twenty-five years. Statistical reports of the different operations reflect a wide variety of choice on the part of individual operators, with no universal lessening of the percentage of failures.

If one cannot feel satisfied with the present status of initial operations for glaucoma, one must feel still more inadequate when confronted with the necessity of a secondary operation.

After the first operation the eye is no longer the same. Its anatomy has obviously been altered. The physiology of secretion and drainage, which depends so much on the integrity of the nervous and vascular systems, has suffered a profound shock. The patient himself cannot be ignored, for in its broader aspects the psychosomatic interrelationship plays its part in the production of glaucoma and certainly in the behavior of the glaucoma in the postoperative state.

If careful, prolonged study of the anatomic structure and reactions of the eye should precede a primary operation, it must be accepted as equally important, perhaps more so, when a secondary operation is contemplated. After a secondary operation it becomes a matter of dealing specifically with the complications that have arisen or of trying to reduce the tension in some other way.

The most optimistic reports of antiglaucoma operations list 10 per cent failures, whether or not the after-treatment involves medication. The period before the return of hypertension varies from a few weeks to many months. Schoenberg's case in which the hypertension returned after eighteen years can hardly be listed as an instance of operative failure!

Errors in judgment naturally increase the number of failures, but even when the operation is well chosen and technically sound, failures occur. Then the cases are analyzed, and the student is presented with an overwhelming number of reasons to account for the failures. Most of the evidence comes from the pathologic laboratory. Lately, with the more universal use of the gonioscope, the young ophthalmologist has learned to look for the reasons for failure in the living eye. In this search, too, the literature will help him, with its many references.

But there the matter seems to stand. The patient still has glaucoma. Medication, then operation and then postoperative treatment have failed. What should be done? The literature is strangely quiet on this question, and the operator has the awful feeling that he is now entirely on his own, God help him!

The subject of reoperations seems important enough to warrant discussion. Every ophthalmologist of experience has been faced with the problem and expects to have it recur again and again, but human nature is reluctant to publish its failures, and the results of experience in this matter have seldom been committed to the printed page. In view of the paucity of material, the approach to the subject is not easy. What little can be said, therefore, must be limited to a few personal experiences and conclusions and the results of conversations with others.

The tension is hardly expected to become normal immediately after operation. As soon as the eye is opened and the pressure drops, there is edema of the ciliary body, and even though an attempt is made to "stabilize" the pressure by the injection of air or saline solution and the use of water-tight sutures, a normal condition does not exist. The eye must be allowed a decent interval to adjust itself to its altered anatomy and physiology. A slight postoperative rise in tension should certainly cause no alarm, and no one would be importunate enough to rush into a secondary operation.

But when the need does arise, a pathologic tension must be combated by whatever measures seem appropriate.

The following case serves to illustrate the unusual amount of operative intervention that sometimes seems justified. Moral support was obtained through repeated consultations with other ophthalmologists, who concurred in the proceedings.

Mrs. F. D., a white woman aged 56, had a Lagrange sclerectomy with peripheral iridectomy for chronic noncongestive glaucoma. The operation appeared satisfactory, but twenty-four hours later the anterior chamber was completely filled with blood. A rise in tension was feared, but the Schiötz tonometer readings were not above 23 mm. of mercury for ten days. Then the eye became stony hard. Irrigation of the anterior chamber through a large corneal keratome incision washed out most of the blood, and clot forceps removed the remaining clot.

The eye quieted down almost immediately, and the tension stayed around 19 mm. of mercury for nine days. Then development of a low grade iritis with posterior synechias necessitated intensive treatment with mydriatics, during which the tension went up to a new high. It was brought down by paracentesis repeated twice a day for a week. The synechias were still present.

It was felt that no real progress was being made, and so the eye was opened again at the site of the original Lagrange operation. The sclerectomy incision was still patent, and through it the iris adhesions were pulled free. The peripheral iridectomy was made complete and the temporal pillar incarcerated in the sclera.

The eye finally quieted down, and later ophthalmoscopic examination disclosed the remains of a large hemorrhage into the vitreous. In view of this final discovery, it is doubtful whether the eye had much of a chance after the blood filled up both the anterior and the posterior segment.

It is not pleasant to report such a failure, but to do so will serve a purpose. It was not known at the time what else to do, nor is it easier in retrospect to decide whether something else should have been done.

Undue hemorrhage is always a matter of concern. When it occurs in the anterior chamber and produces an inordinate rise in tension it can be dealt with in the manner described. In lesser amounts it may respond to medication.

When there is a posterior nonexpulsive subchoroidal hemorrhage, the blood accumulates rapidly and the eye becomes hard and painful. The anterior chamber is usually shallow. According to laboratory reports this type of hemorrhage occurs most commonly after trephining or after the Lagrange type of sclerectomy-iridectomy.

probably because the prolonged softness of the eye permits a rupture of the diseased blood vessels due to removal of the supporting intraocular pressure. Immediate posterior sclerotomy was effective in 2 cases at the New York Eye and Ear Infirmary in removing the blood and saving the eye. The Graefe knife was plunged in, twisted and withdrawn. Other operators report using a trephine operation or dissection to remove a piece of sclera, exposing the choroid. Then multiple diathermy punctures released the fluid. Incidentally, this same procedure (posterior sclerotomy) has been used as an adjunct to the main operation, to reduce the tension posteriorly before the anterior segment was opened.

Except when there is early hemorrhage, the eye operated on deserves a rest. Sedatives, medication applied locally and massage will usually control the tension during the immediate postoperative period. Later, even when the tension is just above normal and persistently refuses to come down, an extensive reoperation need not always be considered. In several cases at the Infirmary a corneal paracentesis or anterior sclerotomy with a keratome has apparently given just the necessary amount of easement to allow the eye to take care of itself.

If a primary operation is necessary, a reoperation is just as much needed when there is a mechanical failure of the first.

There are two main reasons for the failure of an external fistulizing operation: blocking of the filtration wound on the inner aspect of the eye and fibrosis of the overlying tissue.

The filtration wound is blocked most commonly by ciliary processes and iris tissue, sometimes by lens capsule or other debris and sometimes by the products of inflammation. The surprising thing is that so few eyes appear perfectly normal in the area operated on, as shown by gonioscopic studies.

The presence of uveal tissue in the wound is not necessarily an impediment to filtration (as a matter of fact, many ophthalmologists believe that it is a requisite to good drainage), but when it blocks the wound it vitiates the operation. Often when a knuckle of iris fills the opening, drainage can be reestablished by excision of a small piece.

For the past two years, in every case of operative failure in the Knighton clinic at the New York Eye and Ear Infirmary I have examined the patient personally in an attempt to discover the reason for the failure and in the hope that some remedy simpler than another extensive operation could be devised. In perhaps a dozen cases, about equally divided between trephining and sclerectomies, the original conjunctival flap was redissected down to the filtration opening, and if any plug was found in the hole it was removed. The results were almost 100 per cent successful as far as the scleral drainage was concerned. The subconjunctival drainage was another matter. It has long been known that the prognosis is poorer after secondary operations, especially when dissection is made through healed tissue.

Even in primary operations, special emphasis has been placed on the necessity for dissecting the conjunctival flap close to the sclera under Tenon's capsule. This is supposed to allow better absorption of the aqueous, in the looser subconjunctival tissue that lies over the capsule. In spite of the most meticulous care in such dissection, many fistulizing operations fail because of fibrosis of the conjunctival flap. It was surprising to note in a number of eyes in which the incision was reopened, that the trephined hole or the sclerectomy opening was still patent. In each case, however, scar tissue was encountered at the exit of the filtration opening.

The reoperation of course only made matters worse by causing more scar formation.

The injection of an 0.1 saline solution at the primary operation may or may not prevent too firm an adhesion of the conjunctiva.

Injection of air is reported in 1 instance to have reopened the subconjunctival spaces enough to obviate the necessity for further operation. My experience in 1 case was not successful.

When the conjunctival wound is opened with a spatula, the tension stays down from two to five days before the wound is sealed off again. This procedure has been performed in several cases as an office procedure to carry the patient over until a secondary operation could be performed, but there can be no hope of permanent success from repeated traumatism of this sort.

In 1 case a horsehair seton was tried in the area operated on but with no better results. Its use seemed to delay the cicatrization of the conjunctiva a little longer, but that was all that was accomplished.

The patient was a white man 60 years old with chronic congestive glaucoma. A Lagrange sclerectomy and complete iridectomy failed to relieve the hypertension, although redisection of the conjunctiva disclosed a scleral opening that was draining nicely. There was diffuse scarring of the conjunctival flap. A horsehair seton was inserted under the conjunctiva at the sides of the scleral opening and run laterally on each side, as close to the sclera as possible and under conjunctiva that had not been dissected previously. The free ends were buried. It was hoped that the seton would keep a path open to the fresh conjunctiva, but the experiment failed miserably. In eyes not previously operated on, the seton has given better results—even in 2 cases of absolute glaucoma.

The question of repeating the operation is always present. Should the same operation be tried again, or should one choose another type on the assumption that the first one failed because it was the wrong choice?

The answer is not easy. When an apparent choice was offered, the operator undoubtedly selected the original operation because it was the one in which he had the greatest skill and the most confidence. If he was asked to perform a less familiar secondary operation on the simple grounds that the first choice had failed, he would be justified in asking why. On the basis of the operator's ability alone, the eye would probably be safer under a repetition of the procedure in which he was most expert. And if there were technical errors or complications that could be avoided, a second performance would seem justified. But if the original operation was performed to the best of the operator's ability and there were no complications, a failure would mean that the operation was not good enough. It is difficult to know in such cases whether the fault lies with the operator, with the type of operation or with the reaction of the eye in question. But the evidence of failure seems to indicate some kind of error and the necessity for a change. A good operator has more than one string to his bow and is ready to try another when the first gives poor results.

Of the external fistulizing operations, trephining is the first choice, followed by sclerectomy and iridencleisis. The same order of preference seems to obtain in the matter of secondary operations, although some operators prefer a sclerectomy when there is an exacerbation of the glaucoma itself, in contradistinction to inadequate drainage from the incision made in first operation.

When there are signs of irritation with the return of hypertension, cyclodialysis should not be considered as a secondary operation, but a complete iridectomy should be included in the operation selected. Cyclodialysis is often satisfactory as a secondary procedure, especially in aphakic eyes, but it should not be attempted unless the angle is partially open.

There has been a recent swing in favor of iris inclusion operations either alone or in combination with sclerectomy, even as reoperations. My experience, however, has indicated that the best results are obtained when the iris tissue is healthy and not inflamed. In glaucoma of long standing the results have been poor.

The choice of a site for a secondary operation deserves careful study. Transillumination of the eye often prevents later embarrassment by disclosing the atrophic parts of the iris to be avoided, and the scleral scatter outlines the ciliary body. Gonioscopic examination is of course indispensable.

The presence of trabecular or scleral iris adhesions often moves the angle so far forward that trephining into the anterior chamber is impossible. Trephining through the iris into the posterior chamber may succeed, but there is always the chance of incarcerating ciliary processes. If the operation is not spoiled mechanically, it may fail later as a result of a low grade uveitis from irritation of the ciliary body. A Lagrange type of iridosclerectomy in the same circumstances would be impossible.

I have obtained some success by making a horizontal scleral incision with a scalpel just behind the limbus and entering the eye as in iridectomy *ab externo*. The iris is freed from the anterior scleral lip enough to permit a sclerectomy with scissors. Then a small piece of iris is excised. A conjunctival flap has previously been laid down in the usual manner. In 2 recent instances a small amount of fluid vitreous escaped, but except for a continued low tension, about 12 mm of mercury, there have been no untoward results.

Postoperative hypotony may reach serious proportions and has been reported corrected by the bringing down of a conjunctival flap over an area of denuded cornea. The subsequent fibrosis is usually sufficient to elevate the tension. Good results following the application of a thermophore to the filtering bleb have been reported.

A shallow anterior chamber is difficult to handle, and it is not always made deeper by posterior sclerotomy, as some advocates claim. My attempts to open the angle by injection of the anterior chamber with air or saline solution have met with indifferent success. Preference is still held for the *ab externo* approach. In several private cases a swollen lens was removed with good effect on the tension and a deepening of the anterior chamber. In one of these the extraction was carried out through an old glaucoma filtration wound, destroying its effect, but the tension remained normal. The same procedure in a clinic case caused a postoperative return of the hypertension, which had to be controlled by another operation. The lens should be removed in capsule whenever possible to avoid later blocking by lens or capsular debris.

In spite of all precautions and attempts to prevent absolute glaucoma, in many eyes this condition develops. For it, of course, the perfect reoperation is enucleation, but when the patient protests, the surgeon must temporize. Simple posterior sclerotomy will often relieve the pain, although it seldom effects a permanent reduction in tension. Diathermy puncture through a posterior scleral trephine opening has been reported to give the same result. Opticociliary neurectomy has been effective in relieving the pain, and injection of alcohol into the ganglion has produced the same result. Perhaps other measures can be justified on the basis of expediency.

These are a few of the secondary attempts that have been made to rectify an initial operative failure. Many other methods have been tried with varying success but have not been mentioned because of lack of familiarity with them.

SUMMARY

Reoperations are necessary in the treatment of glaucoma because primary operations are not always successful

Except when obvious faults of the primary operation can be corrected, a reoperation has less chance of succeeding because of physiologic changes, mechanical difficulties, fibrosis or other unknown factors

Any operation is a decided shock to the eye and its functioning, the post-operative state may differ widely from the preoperative state and requires careful restudy before further intervention is considered

The subject of reoperations deserves more discussion than it has received

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FIXATIONAL CORNEAL LIGHT REFLEXES AS AN AID IN BINOCULAR INVESTIGATION

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MEDICAL CORPS, ARMY OF THE UNITED STATES

The estimation of binocular imbalance based on objective examination of the eyes has been found unsatisfactory because inspection of the eyes in a routine examination of the muscles is often difficult. The role of the corneal light reflex as an aid in clinical practice has not been sufficiently explored, and my aim in this paper will therefore be to show how this reflex can be utilized clinically to complement the familiar cover test.

First, as to the meaning of the fixational corneal light reflex. For practical purposes it may be regarded as the constant position of the light reflex on the cornea when the eye is made to fix a light and when the observer's eye is behind the testing light. It may not be on the center of the cornea (angle gamma), even though the macula assumes fixation, but it represents the normal anatomic position of the light reflex for that fixing eye and is to be distinguished from the more peripheral, or deviational, corneal reflex seen in a squinting eye when the fellow eye is fixing.

With an ordinary flashlight one notes whether fixation is as satisfactory binocularly as monocularly. The examiner keeps his eye directly behind the test light and makes a mental note of the position of the light reflex on both corneas. He then covers each eye alternately and compares the binocular reflexes with reflexes obtained by monocular fixation. If the corneal light reflexes assume the same positions binocularly as they do on monocular fixation, deviation is absent for that testing distance. Displacement of the light reflex from the fixation position in one eye when both eyes are tested indicates deviation in that eye. If the reflexes appear centered on binocular stimulation but displacement occurs in one eye on attempted monocular fixation by the alternate cover test, false macula is suggested.

If one regards a fixational corneal light reflex as defined as indicating normal macular projection, displacement of the light reflex from the fixing position would indicate registration of the image on an extrafoveal portion of the retina. If a light is directed on the cornea from the nasal side so as to produce a corneal reflex medially, registration of the image on the retina will be temporal. One may simplify matters by stating that the position of the corneal light reflex in relation to the fixing position indicates the direction in which the image is being projected (fig. 1). If the reflex is nasal to the fixing position, projection of the image is also nasal.

In terms of binocular imbalance, the corneal light reflex in divergent squint would be nasal in the deviating eye, or in a direction opposite to the deviation, and diplopia, if present, would be nasal, or crossed, to correspond to the nasal displacement of the reflex. When the reflex is displaced upward and nasally while the other eye fixes (fixational reflex), there is a downward as well as an

outward displacement of the eyeball (hypoexotropia), an inferotemporal registration and, again, an image projection (upward and nasalward) corresponding to the displaced position of the corneal light reflex in relation to the fixing position

To appreciate more fully the meaning of a corneal light reflex one should bear in mind the following principles

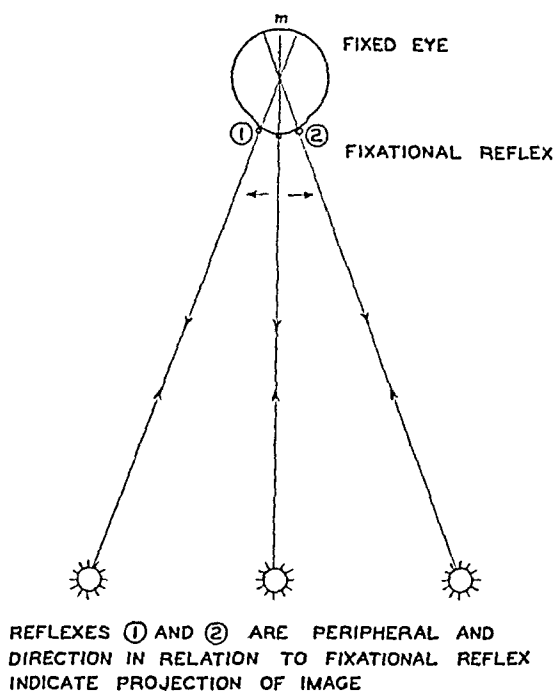


Fig 1—Position of the corneal light reflex indicates image projection

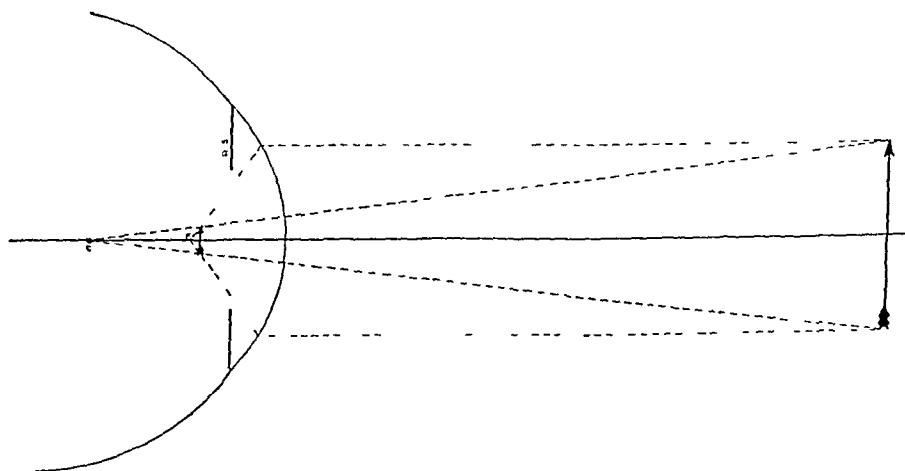


Fig 2—Relative size and position of image with convex mirror

A The apical portion of the cornea is a convex spherical mirror and therefore the first, or anterior corneal, reflex has all the characteristics of an image produced by such a mirror (fig 2)

B The corneal light reflex is diminished in size, erect and virtual

C Any ray incident through the center of curvature will return along the same path. An incident ray parallel to the principal axis will be reflected as coming from the focal point, which is located one half of the radius behind the surface

D Owing to the relatively small radius of the cornea (about 8 mm), the image plane for any test light distance will practically coincide with the focal plane 4 mm behind the surface. Even if the test light is 333 mm from the cornea, the difference in location is only 0.05 mm.

E The anterior, or bright, Purkinje corneal reflex, therefore, strictly speaking is not a superficial reflex, but is retiocorneal, or 3 to 4 mm behind the surface.

F As a light is moved parallel to the facial plane of the patient the corneal light reflex moves in the same direction, although to a much reduced extent.

G The position of the corneal light reflex depends on the position of the test light relative to the principal axis and the eye of the observer. The distance from the test light to the cornea is of no practical influence, for the reasons mentioned.

It is important for purposes of accuracy to adopt a uniform means of studying corneal light reflexes. The position of the examiner's eye behind the light source is found to be most reliable and uniform.

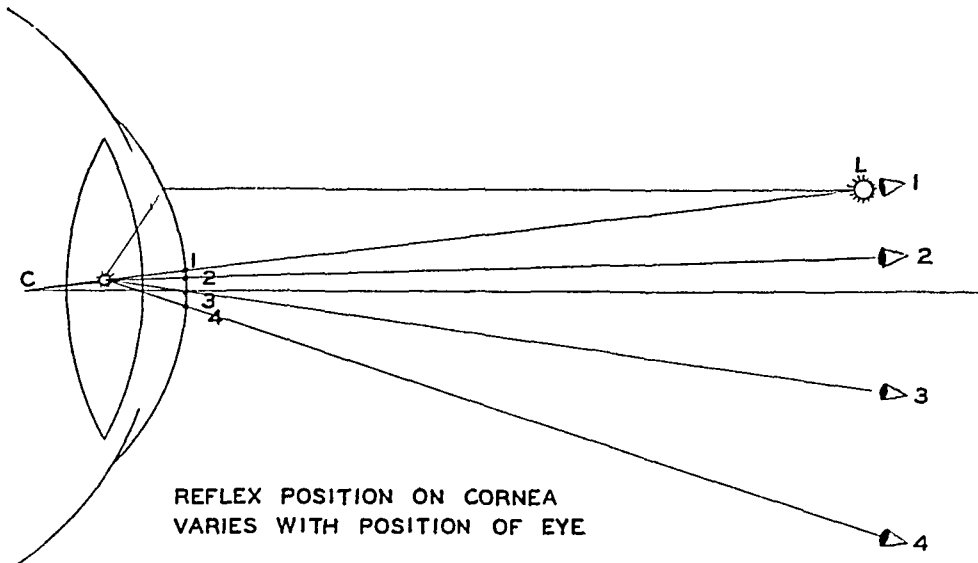


Fig. 3—Hirschberg reflex.

If one assumes that fixational corneal light reflexes indicate an absence of deviation, one can reason that any artificial means of centering a peripheral corneal light reflex, as in squint, might likewise serve as a basis for measuring ocular deviation. In the case of the synoptophore, the carriers are rotated until they are in direct line with the corresponding fixation positions on the corneas, and readings are made. This is a far more satisfactory method than the crude Hirschberg test, based on translating roughly the position of the corneal light reflex in a squinting eye in terms of millimeter displacement from the fixing position.

The method involving the peripheral corneal light reflex (Hirschberg, fig. 3) is unsatisfactory for the measurement of squint because

- 1 It is based on a rigid value (8 mm) for the corneal curvature, which must vary in different persons.

- 2 It is difficult to control the patient sufficiently to measure the position of the light reflex accurately. Moreover, the position of the reflex changes with movement of the examiner's eye.

- 3 The amount of millimeter displacement can be estimated only roughly and is never found to be uniform when measured by different examiners. Moreover,

a displacement of only 1 mm means 7 degrees, and one is in no position to make fractional readings

4 The method does not take into account the center of rotation of the eyeball in addition to the center of curvature of the cornea

5 The corneal curve is not a geometric curve, because flattening toward the limbus takes place

6 A corneal light reflex seen peripherally is distorted, whereas one seen at the center of the cornea is sharp

Artificial restoration of fixational corneal light reflexes for measurement of ocular deviation may be obtained as follows

1 By ordinary flashlight In convergent squint, the light reflex on the nonfixing eye will be displaced temporally from the corneal fixation point As the test light is gradually moved along a rule closer to the eyes, the light reflexes reach the corneal fixation points, and on the basis of the patient's interpupillary distance and the distance of the light from the eyes (near point of convergence), one can calculate readily the amount of squint In actual practice, however, this method of testing convergent squint is found wanting One must be careful to stop just at the position at which the lights appear centered, or an added convergence impulse may upset one's reading, measurement of the interpupillary distance in a patient with convergent squint may prove difficult, and, finally, the reading obtained can be interpreted as the deviation for that distance only and not for 20 feet (610 cm) or 13 inch (33 cm) test distances

2 By means of a partition, or septum, and individual test lights at a set distance between the eyes A light on one side of the septum is set in front of the fixing eye, while the light on the other side, for the nonfixing eye, is moved laterally or vertically or both until it, too, produces a light reflex on the corneal fixation point When this position is reached, alternate fixation to light stimulation should produce no movement of the eyes unless amblyopia is present in the nonfixing eye The examiner's eye should be behind the test light

A septum placed between the eyes serves the purpose of a cover but with the difference that the two eyes can be observed at the same time In orthophoria the two eyes project to a common point on the cover test When the cover is moved into a septal, or between the eyes, position, fixation by one eye on a corresponding light placed close to the septal wall will make the fellow eye converge in the direction of the unseen light in the case of orthophoria In exophoria or exotropia the nonfixing eye turns out, and the test light is displaced laterally to reach the corresponding corneal fixation point In esophoria or esotropia the light reflex on the deviating eye is displaced laterally to the fixation point, and supplementary base-out prism is required to center the light reflex in the deviating eye

Use of the septum arrangement is of distinct advantage not only as a quantitative cover test but as a comprehensive means of comparing objective and subjective responses, notably in cases of abnormal retinal correspondence When the images appear to touch or to correspond at the angle of deviation, it speaks for so-called normal retinal correspondence because the subjective, or image, angle corresponds with the objective, or deviation, angle

3 By means of the synoptophore or the stereoscope The synoptophore and the stereoscope are essentially devices which utilize the principle of the septum, or independent stimulation to each eye They also incorporate plus lenses to relax accommodation and convergence, thus bringing parallelism of the visual axes to

within a comprehensive range. Whereas without the septum the eyes normally tend to converge on opposite sides of the septum, the incorporation of plus viewing lenses tends to shift the visual axes outward.

The basis for centering of the corneal light reflexes with the synoptophore appears simple. By rotation of each carrier around a pivotal point the mirrors are so rotated as to bring the corneal light reflexes to their respective fixing positions at the angle of deviation.

With the Brewster stereoscope¹ a critical corneal light reflex can likewise be obtained by use of bright transparent targets that do not cover too large retinal fields. As these targets are placed in the calculated primary positions for different accommodations one may readily note whether centering of the corneal light reflexes is maintained. The angle through which such targets are displaced medially or laterally relative to the primary positions in order to strike the centers, or fixation

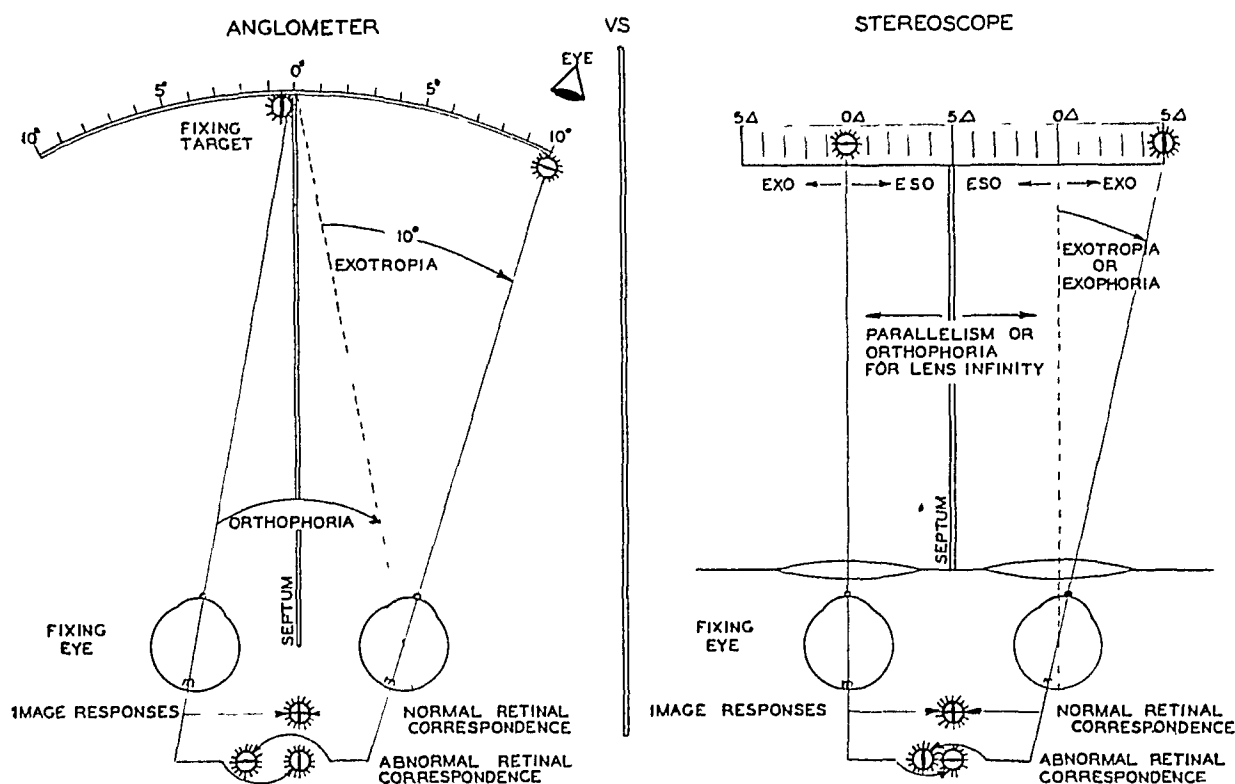


Fig. 4—Comparison of anglo-meter and stereoscope, showing positions of targets in relation to ocular deviation, fixational corneal light reflexes and image responses.

points, of both corneas serves as a measure of the amount of ocular deviation for that testing distance.

The anglo-meter,² also incorporating a septum, provides for studies of the corneal light reflexes at but one accommodative range (3 D), or at a fixed distance of 13 inches (33 cm), its flexibility lies in its permitting one to study the positions and visual responses of the eyes in the different motor fields. My stereoscope permits one to study the corneal light reflexes in a single motor field or with the eyes-front gaze, but its flexibility lies in its enabling one to study the corneal light reflexes at different viewing distances or accommodative ranges.

1 Krinsky, E. The Stereoscope in Theory and Practice, *Brit J Ophth* **21** 161-197 (April) 1937, Some Newer Developments in Precision Type Stereoscopes, *Arch Ophth* **19** 394-402 (March) 1938, Modifications of the Brewster Stereoscope for Clinical Requirements, *ibid* **26** 808-815 (Nov) 1941.

2 Krinsky, E. The Cardinal Anglo-meter, *Arch Ophth* **26** 670-674 (Oct) 1941.

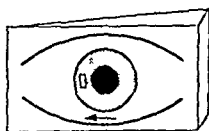
4 With the aid of a prism—the prism reflex test In the routine study of ocular deviation a prism is used to nullify ocular motion on alternate covering. The role of the variations in the position of the corneal light reflex as a result of use of the prism has been largely overlooked, possibly for the reason that test targets set at a distance of 20 feet are too faint to yield visible corneal light reflexes. In studying the effects of a prism with a test light at a 13 inch reading distance I found that, whereas a ray of light traversing such a prism was refracted toward the base, reflection of the light on the cornea was toward the apex. I found, moreover, that a prism sufficient to stop motion of the eyes on alternate covering also had the fortunate property of centering the corneal light reflexes. This interesting phenomenon, to my knowledge, has not been reported previously in the medical literature. So here there is additional proof that whatever method one employs the primary aim in measuring latent or manifest squint is, first, to

1 WITHOUT PRISM



REFLEX CENTERED WITHOUT PRISM

2 WITH PRISM



LIGHT REFLEX DISPLACED TOWARDS
APEX OR IN DIRECTION OF ARROW
ALTHOUGH LIGHT SOURCE REMAINS
FIXED

Fig 5—Effect of prism on glass eye

produce artificial restoration of the corneal light reflex from a peripheral to a fixing position, and with prisms to ascertain the strength required to center these reflexes artificially.

One can observe easily the change in position of the corneal light reflex with gradual increase in prism by experimenting with a glass eye and a rotary prism. The light is directed to the center of the pupil, and both the observer's eye and the test light are kept in line in a steady position. As the prism is rotated in either direction, it will be noted that the light reflex moves in the direction of the apex of the prism and that a slight increase in strength of the prism will produce appreciable displacement of the light reflex. The eye itself will also be seen to move toward the apex of the prism, but such gross change in the apparent position of the eyeball is distinct from that of the corneal light reflex because it is on a different image plane. One can simulate deviation by turning the glass eye in or out in relation to the test light, which remains in the same position. When the eye is turned out, the light reflex is seen to move in from the fixation

or the central position To bring the light reflex back to the fixation position, one merely sets the prism with the apex in the direction of the center of the pupil Comparison of the setting of the prism to the direction which an arrow must take to reach the center of the pupil simplifies the matter

The prism reflex test simplifies the measurement of ocular deviation The novice confronted with a patient with squint may be at a loss as to how to place his prism in order to neutralize the deviation If he thinks in terms of fixational corneal light reflexes, he merely turns the prism first one way and then the other and notes the direction and amount of prism (using a rotary prism) required to bring the light reflex in the deviated eye to a central position In esotropia the eye is turned in and the light reflex is displaced temporally, and a base-out prism centers the corneal light reflexes accordingly If the eye turns upward as well as inward, the light reflex in the deviated eye is displaced downward as well as outward and both a vertical (base-down) and a base-out prism bring the light to the center of the cornea in that eye

Certain precautions should be observed

A This test is most satisfactory for a 13 inch test range For greater distance, a stronger light source must be employed to yield a bright corneal light reflex

B A rotary prism is the most satisfactory instrument for the test A photometer is generally unsatisfactory, because the framework covers the eyes in such a way as to make careful inspection of the reflexes difficult

C As a rule the prism is placed over the fixing eye, and changes in the position of the corneal light reflex are observed in the deviating eye

If in a case of manifest squint, the corneal reflex is displaced only laterally (horizontal squint), this simplifies prism testing, in that a rotary prism alone is sufficient to produce centering of the corneal light reflexes If the displacement is oblique, in other words the squint is vertical as well as horizontal, one first corrects the vertical component by using a vertical prism, always remembering that the light reflex will shift in the direction of the apex of the prism Specifically, if the reflex in the deviated eye is higher (hypotropia), one first levels the reflexes by placing a prism with the apex down As a rule the vertical component requires much less prism than the horizontal component, and when this correction is disposed of, one is in a position to neutralize the horizontal component with a rotary prism placed in front of the vertical prism The rotary prism is rotated so that the light reflex moves in the direction of the apex of the prism If the reflex in the deviated eye is displaced medially (exotropia), one rotates the prism base in, or apex outward After having obtained what appears to be centering of the light reflexes in both corneas, one supplements the procedure with the familiar cover test and ascertains whether ocular motion has been stopped and whether the light reflexes remain steady on alternate covering It often happens that the results of this rapid preliminary prism reflex test conform closely with those of the cover test In other instances, just a little more turning of the prism in either direction is sufficient to stop the movement At any rate, one sees the eyes and their reflexes much more clearly than one does by relying on ocular movement alone

The prism reflex test does not replace the familiar cover test but simplifies it by permitting rapid inspection of the restoration of the corneal light reflexes to their fixation positions The cover test alone is not infallible, for if one has to rely entirely on the gross appearance of the eyes one may be at a loss to tell exactly when movement has stopped It requires a critical eye to judge cessation

of fine ocular movements, and the prism reflex test proves helpful as a rapid confirmatory test. Also, the cover test is deceptive in certain types of manifest squint associated with false macula, in which there is no movement of the eyes on alternate covering. In this case the prism reflex test offers a satisfactory estimate of the amount of squint.

As a rule, the examiner selects one eye for placement of the prism. I usually place the prism before the right eye. However, in the case of severe squint, especially with amblyopia, one sets the prism before the normal, or fixing, eye and then by rotating it in the direction of neutralization observes the corneal

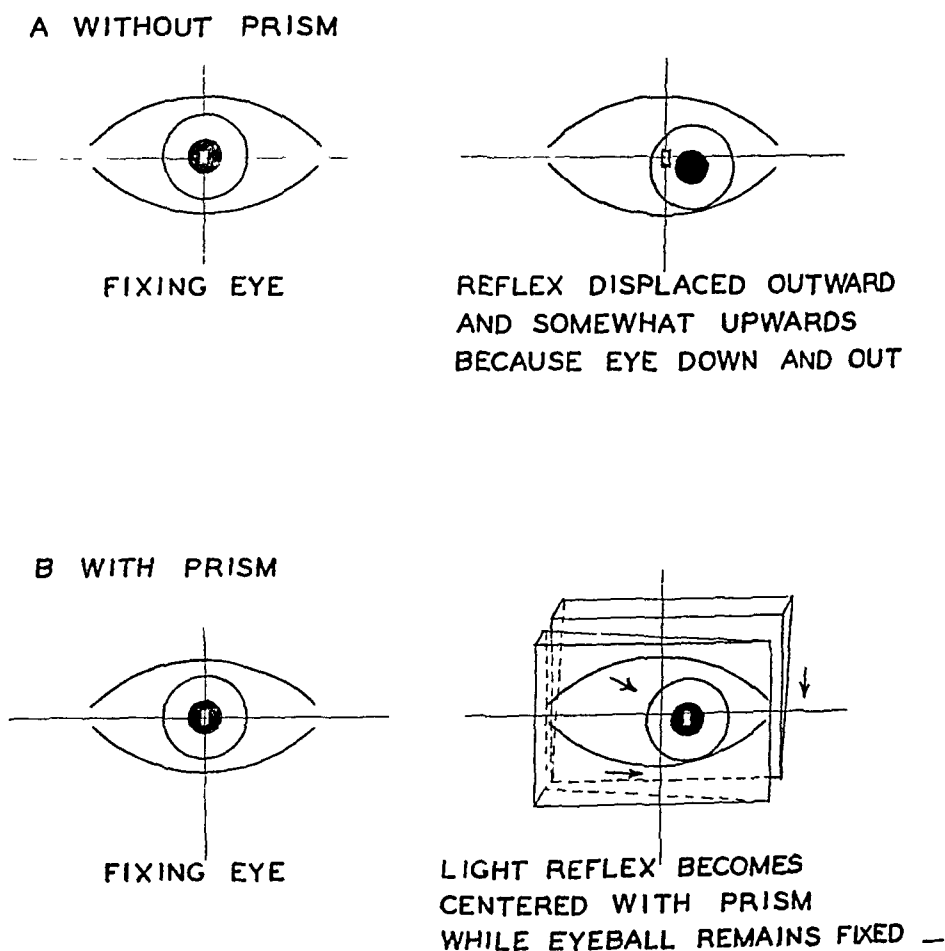


Fig 6—Hypovotropia, showing restoration of fixational corneal light reflexes by prisms

reflex becoming gradually centered in the otherwise deviating eye because the fixing eye moves in the direction of the apex of the prism. For this test I prefer the simple rotary prism to the bulky phorometer, because it covers one eye rather than both, it is free from obstructing framework, it can be used on either eye and it can be used for the study of vergence as well as deviational response. It is also preferable to individual square prisms.

For excessive deviation no prism is reliable, and the angle method as embodied in the cardinal angiometer is the method of choice. The angiometer enables one to study deviations in all selected positions of gaze and has certain controlled features which render the readings reliable. Moreover, it is based on physiologic and optical principles which make it as sound as is feasible for clinical requirements.

CLINICAL APPLICATIONS OF THE CORNEAL LIGHT REFLEX TEST

1 *Pseudosquint, Angle Gamma, Epicanthus*—In studying the corneal light reflexes, one first determines their position on each eye with monocular fixation. Whether the reflex is found centered or somewhat off center (angle gamma), for practical purposes one calls its location the corneal fixation point because it corresponds to macular fixation. In fact, one may disregard the measurement of angle gamma and think of ocular deviation as the displacement of the corneal light reflex from the fixed corneal position assumed on monocular fixation. With both eyes open, binocular fixation would therefore imply the simultaneous registration of the corneal light reflexes on the monocularly fixating corneal points.

By thinking of epicanthus in terms of the corneal light reflexes, one notes the absence of true squint when the reflexes are found centered both monocularly and binocularly.

2 *False Macula and Amblyopia*—False macula, as distinguished from abnormal retinal correspondence, is a form of amblyopia in which monocular foveal fixation is faulty. The corneal light reflex is thus seen to waver as the eye searches over a paramacular area to register imperfectly what the fovea is unable to accomplish. Fixation is unsteady, and the position of the corneal light reflex is not uniform. As a rule, it is displaced temporally in convergent squint and nasally in divergent squint. It may be confused with angle gamma when the light reflex is not centered, but the nature of such fixation should serve to distinguish these two conditions. In some cases the corneal light reflexes appear centered when both eyes are open, but alternate covering will show the nature of monocular fixation and reveal the existence of false macula. In other instances the light reflex may appear centered on attempted monocular fixation, whereas foveal fixation would yield a gamma corneal reflex.

In false macula with visible deviation in the amblyopic eye, one often finds that the eyes fail to respond to alternate covering and the poor eye remains deviated both with and without cover. In such cases testing the corneal light reflex (with prism) proves satisfactory for measuring the deviation. In convergent squint a base-out prism placed over the good eye will make that eye turn in in order to fix the light, and the poor eye will therefore turn out until the light reflex is centered on that cornea as well.

While one cannot judge visual acuity objectively by observing the corneal light reflex, one can with a little experience suspect amblyopia on the basis of the relative unsteadiness of the corneal light reflex in the amblyopic eye. This test is not infallible, but is occasionally helpful, especially when one is dealing with cases of malingering.

3 *Abnormal Retinal Correspondence*—Abnormal retinal correspondence should not be confused with so-called false macula. In the former condition monocular fixation in either eye is not disturbed. However, a perverted relationship exists between the macula of one eye and the paramacula of the other whereby diplopia is avoided. This relationship is interchangeable and exists with either eye assuming the role of fixation.

Abnormal retinal correspondence is a frequent accompaniment of manifest squint. It differs from normal retinal correspondence in that binocular fixation, or fusion, or superposition of images, does not occur when binocular stimulation is made possible through artificial means, such as a prism, stereoscope or angiometer. One can detect abnormal retinal correspondence with any device which provides independent and simultaneous light stimulation to the two eyes.

sufficiently strong to produce satisfactory corneal light reflexes. Measurement is based on movement of the lighted targets along a calibrated arc (as in the angiometer) or graduated bar (as in the stereoscope) until they are in line with the respective fixing positions of the corneas. After the examiner notes the objective angle on the basis of such artificial centering of the corneal light reflexes and subsequent cessation of ocular movement on alternate flashing, the patient notes whether the images appear to touch. Approximation of these independent images at this deviation or objective angle speaks for normal retinal correspondence. Appreciable displacement of the images suggests an abnormal response, or so-called abnormal retinal correspondence, and the lighted targets are moved until their images approximate or cross at this new, or subjective, angle, and readings are again made. Thus in exotropia the images would appear to coincide not at the angle of the squint but at some angle nearer the "O," or primary position, like-

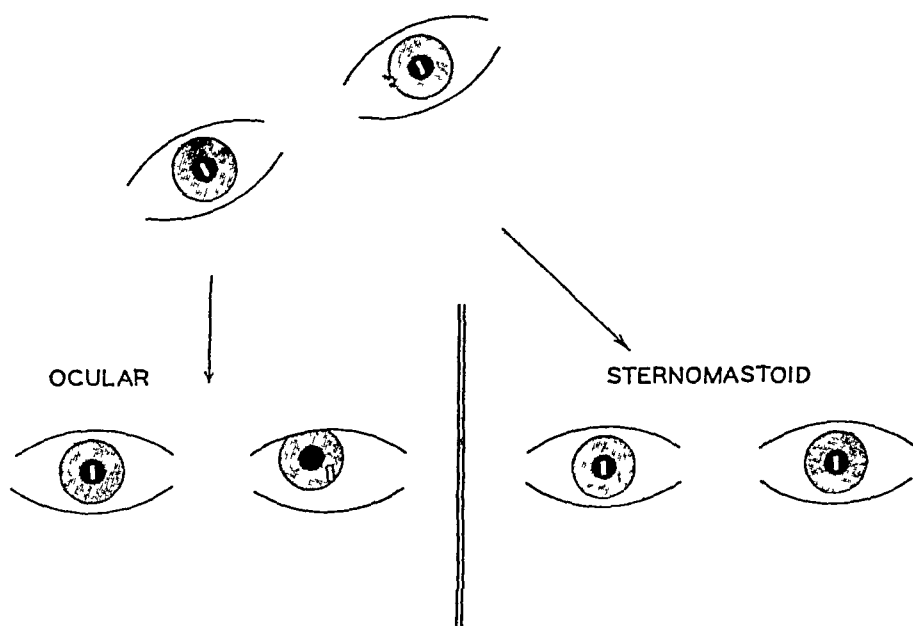


Fig 7—Ocular versus sternocleidomastoid torticollis

wise, in esotropia the images appear to coincide at a less convergent angle than the deviation angle (fig 7)

4 *Ocular Torticollis*—Tilting of the head normally does not result in binocular imbalance or diplopia. In spite of such positional changes of the head, the corneal light reflexes remain centered. This objective manifestation of normal binocular responses proves helpful in indicating whether a head tilt is ocular or orthopedic in origin.

In a case of habitual head tilt, for the corneal light reflexes to remain centered when the head is straightened suggests that the condition is not ocular in origin. In ocular torticollis, the reflexes are centered only in the position in which the eyes can see binocularly. In other positions of the head, the light reflex is displaced in the nonfixing eye, and its position in relation to the position of the corneal reflex in the fixing eye suggests the nature of the diplopia and of the deviation.

5 *Cardinal Positions of the Eyes*—Owing to the asymmetric conformation of the upper lids one is never certain from a cursory inspection of the eyes in the

oblique positions of gaze whether or not paralysis of a levator or a depressor muscle exists. Alternate covering of the eyes may not prove feasible, especially with an uncooperative patient. However, in observation of the corneal light reflex one is often surprised to learn at a glance that what appears to be a lag or paralysis of the superior rectus muscle is a false alarm due to the uneven conformation of the lids. This pseudosquint is analogous to the epicanthus simulating convergent squint.

In a routine examination with an ordinary flashlight, the movement of the examiner's eye when he is testing the eyes in the oblique positions proves clumsy, because his eye must keep moving behind the flashlight to obtain uniformity in response. However, in the Bielschowsky method, the head is tilted in different positions to produce the effects of oblique gaze, and the examiner can maintain his own head in a uniform position by operating the test light from a set position.

The cardinal angiometer lends itself quite satisfactorily to controlled measurement and inspection of the light reflexes for definite positions of gaze. Some patients may not be in a position to move their eyes obliquely upward or downward for more than a few degrees. It makes a difference if one's readings are based on an upward gaze of 30 or one of 10 degrees. With the angiometer one is in a position to note accurately the variations in imbalance with different selected positions of gaze, as well as the limits of oblique gaze. The head is kept fixed in a head rest, so as to prevent instinctive turning with movements of the eyes. Measurements can be made in but a fraction of the time required to make crude readings with prisms, and the test distance is fixed at 13 inches (33 cm) in all directions of gaze. With prisms one is never certain of one's operating distance, instinctive head tilt cannot be properly controlled, and multiple prisms are not simple to manipulate. Also, with marked deviation the reliability of prism readings drops sharply, whereas angle readings conform to the angular deviations of the eyes along an arc.

6 *Fixing Eye*—When a test light is brought gradually closer to the eyes so as to elicit convergence, a point is reached at which convergence is "broken" and one eye turns out and its reflex becomes displaced nasally. This is the nonfixing eye. When the corneal light reflex assumes a different position on alternate monocular fixation (with the cover test) than on binocular stimulation, one may assume that the eye which maintains the same position of the corneal light reflex with both binocular and monocular stimulation is the fixing eye.

7 *Near Point of Convergence*—When a light is taken gradually nearer to the eyes an impulse to convergence is brought automatically into play, and one determines the proximal termination of the range at which the fixational corneal light reflexes can be maintained, or the near point of convergence. This is also the distance at which displacement of the reflex on one cornea occurs. The test is a simple objective one, and the examiner can note the "break" and foretell the nature of the diplopia.

8 *Prism Convergence and Prism Divergence* (fig. 8)—The amount of base-in or base-out prism which one can overcome with a rotary prism is a measure of the prism divergence or prism convergence. The prism reflex test lends itself satisfactorily to revealing to what extent the fixational corneal light reflexes can be maintained. A displacement of the light reflex from the fixation position as a result of an increase in the strength of the prism indicates a "break" in fusion and is of objective value in cases of suspected malingering when the fixational

reflexes are maintained in the presence of a moderate increase in the strength of the prism

In routine prism tests one often relies on the patient to say when fusion is "broken" and, in overlooking the objective value of the prism reflex test, fails to realize that what appears to be fusion or compensation for the prism is in reality relative suppression in one eye. In such cases, the light reflex will keep shifting in the nonfixing eye as the strength of the prism is increased until stimulation of a more sensitive zone beyond the suppression area produces diplopia.

9 *Objective Heterophoria*—A prism (say 10 prism diopters base down) placed vertically over one eye ordinarily causes vertical diplopia. The nature of such vertical diplopia depends on whether one is dealing with orthophoria, esophoria or exophoria. In orthophoria (fig 9) the position of the eye is not changed by the

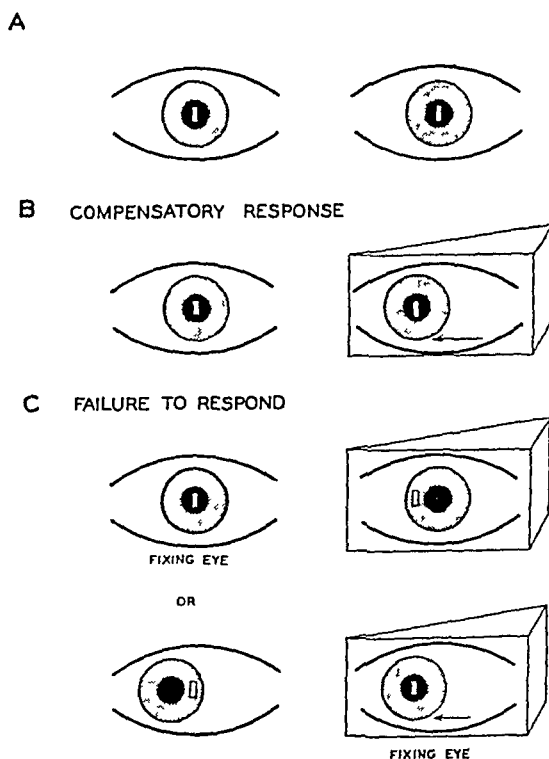


Fig 8—Prism convergence, with maintenance of fixational corneal light reflexes

vertical prism, and the light reflex is displaced vertically, or in the direction of the apex. If the eye behind the prism is the nonfixing eye, the light reflex is higher and the false image created by the prism is also higher than the image seen by the fellow, or fixing, eye. If the patient transfers fixation to the higher image by turning the eyes upward, the light reflex becomes centered in the eye behind the prism and correspondingly lowered in the otherwise fixing eye. The displacement of the light reflex in either eye suggests diplopia, especially when alternate vertical fixation occurs. The nature of such displacement indicates the type of diplopia as well as the nature of the heterophoria.

In esophoria (fig 10) the nonfixing eye turns in behind the vertical prism, and, in addition to vertical displacement of the corneal light reflex toward the apex by the prism, there is a temporal displacement as a result of the turning in of the eye. The position of the displaced light reflex indicates the nature of the

false projection and, incidentally, the type of heterophoria. From the standpoint of measurement, that amount of lateral prism which will bring the light reflex into a straight, vertical position or into an orthophoric position also serves as a measure of the amount of esophoria. By such vertical realignment of the dual reflexes the images likewise become vertically realigned.

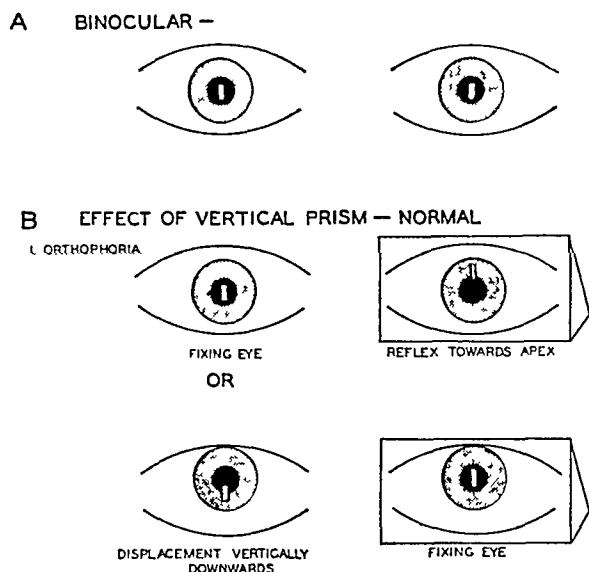
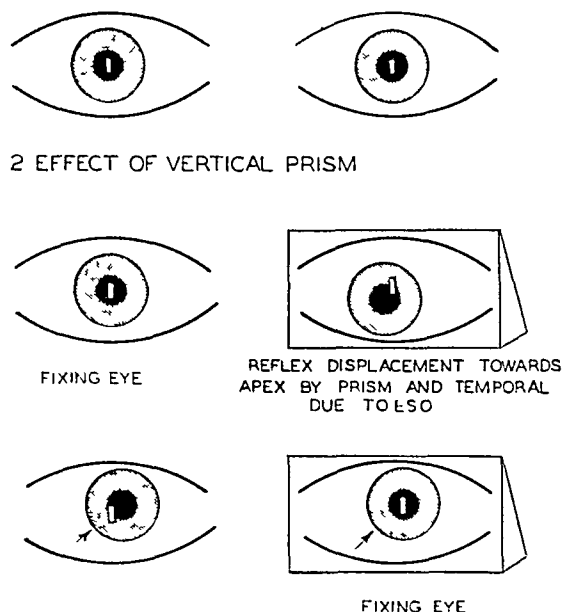


Fig 9—Vertical prism in orthophoria



3 EFFECT OF ADDED BASE OUT PRISM

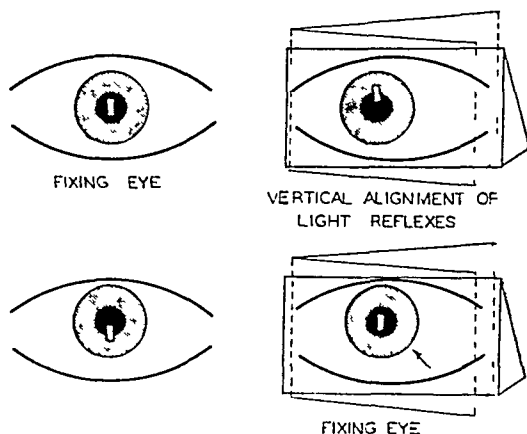


Fig 10—Esophoria and restoration of vertical corneal light reflexes by a neutralizing base-out prism

In exophoria, the nonfixing eye turns out behind the prism, and the corneal light reflex is displaced inward as a result of the heterophoria and upward as a result of the vertical prism. In this condition, too, the amount of base-in prism required to restore vertical alignment of the dual light reflexes indicates the amount of exophoria. Also, the oblique positions of this displaced light reflex relative to the fixed position indicates the direction of projection of the false image.

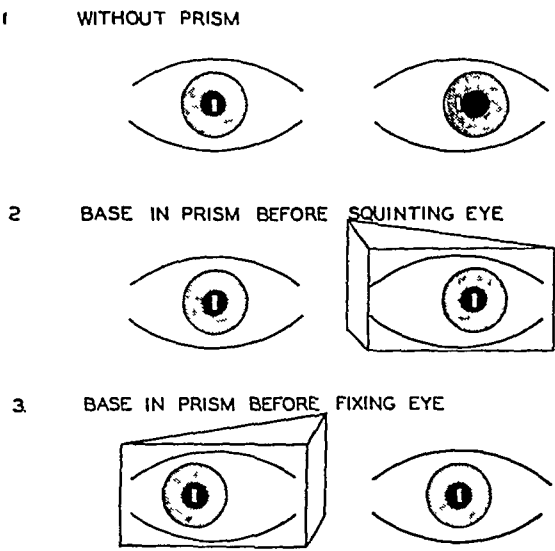


Fig 11—Divergent squint

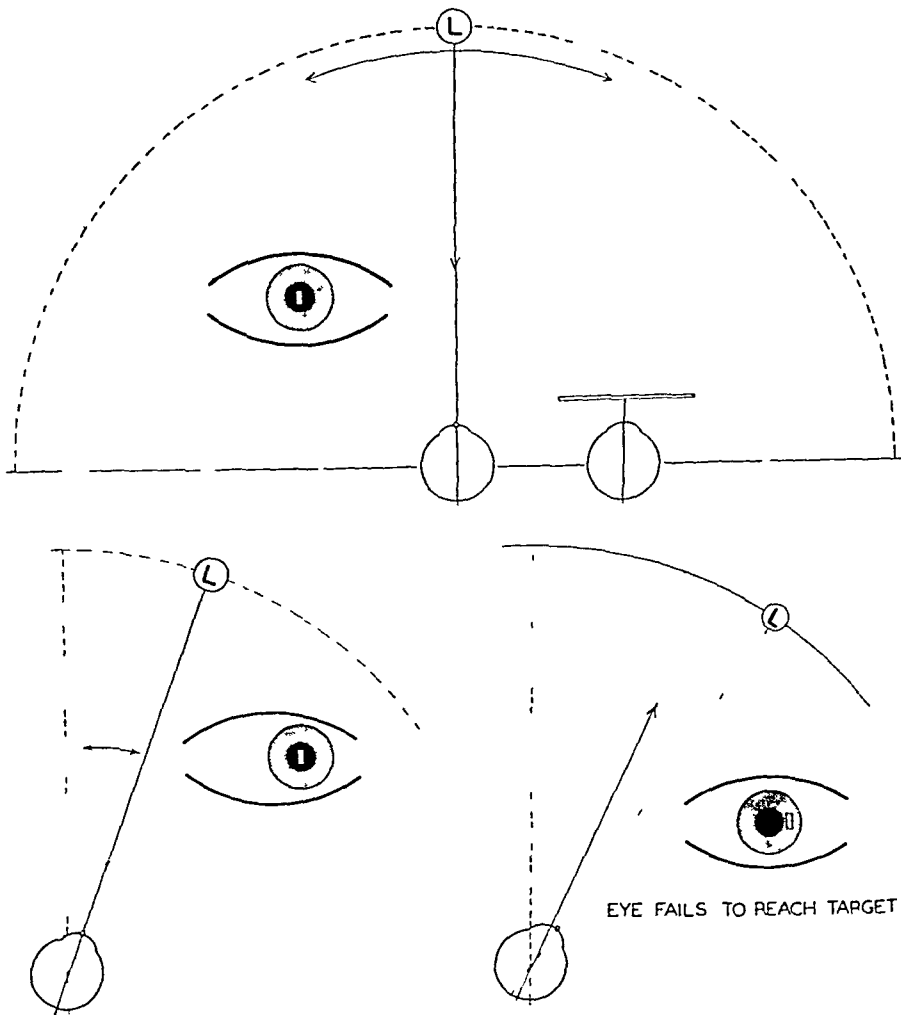


Fig 12—Range of monocular movement as shown by the corneal reflex test

10 *To Distinguish a Heterophoria from a Heterotropia*—In heterophoria, as distinguished from heterotropia, the eyes can respond to certain artificial stresses, such as those due to prisms, and still maintain binocular single vision and fixational corneal light reflexes. In heterophoria (fig 11) the placement of a prism before the fixing eye will merely cause both eyes to turn in the direction of the apex of the prism (conjugate movement) in order for the fixing eye to maintain fixation behind the prism, and the position of the corneal light reflex will change only in the nonfixing eye, the placement of the prism before the nonfixing, or passive, eye will merely serve to move the light reflex in that eye, without altering the position or movement in either eye. In either condition, the amount of prism required to neutralize the deviation will also serve to bring the corneal light reflexes to the fixation positions. In heterophoria, each eye will overcome by the same amount the effects of a prism and still maintain binocular single vision (fixational corneal light reflexes).

11 *Paralytic Squint, Primary and Secondary Deviations*—In paralytic squint one seeks to determine (a) the fixing eye, which has the fixational corneal light reflex, (b) the type and amount of displacement of the corneal light reflex in the fellow eye, (c) the changes in displacement of the light reflex in the nonfixing eye as the eyes are shifted in the cardinal directions of gaze, and (d) the amount of induced displacement in the otherwise fixing eye when the nonfixing eye is made to fix.

12 *Monocular Movements* (fig 12)—Observation of the central corneal light reflex is invaluable in objective measurement of the amount of monocular motility.

With the angiometer, the patient's head is placed firmly in a head rest, and the testing eye is brought into a cyclopean position (the other eye covered). The lighted target is moved along the calibrated arc, and the observer notes through what range fixation of the corneal light reflex can be maintained, first in one direction and then in the other. The area of motility can be plotted so as to include both the vertical and the horizontal directions of gaze.

CONCLUSIONS

1 While the cover test rightfully serves as a basis for estimation of both latent and manifest deviations, it is not always easy for the examiner to observe slight movements in each eye on alternate covering.

2 Observation of the peripheral corneal light reflex (Hirschberg) is an unsatisfactory objective test, subject to the whims of the individual examiner.

3 Artificial restoration, or centering, of the corneal light reflexes to their fixation positions is a controlled and graded objective method for measuring ocular deviation and binocular imbalance.

4 Artificial centering of the corneal light reflexes can be obtained by acceptable methods which enable one to study binocular responses. Such methods include prism tests and use of the angiometer, phorometric stereoscope or synoptophore.

5 A prism refracts light toward the base, but displacement of the corneal light reflex takes place toward the apex. In squint, a correcting prism is so placed as to shift the corneal light reflex to the fixation position. The amount of prism required to center the corneal light reflexes also serves as a measure of the deviation.

6 The position of the peripheral corneal light reflex indicates the projection of the false image in the case of diplopia. To overcome diplopia, artificial centering of such reflexes is required. A prism placed with its apex in the direction of the deviation will restore the light reflexes to their fixation positions.

7 The prism reflex test simplifies the measurement of ocular deviation. It is intended to complement rather than to replace the familiar cover test, and is of objective value (*a*) in determining the amount of prism convergence and prism divergence as determined by the extent through which the fixational corneal light reflexes can be maintained with increasing prism, (*b*) in measuring heterophoria, (*c*) in distinguishing a heterophoria from a heterotropia, (*d*) in measuring squint with severe amblyopia and (*e*) in demonstrating malingering.

8 A rotary prism is the most satisfactory prism device for observation of the gradual correction from peripheral to fixational corneal light reflexes in manifest squint.

9 The refined Brewster stereoscope enables one to center the corneal light reflexes at the angle of deviation. Moreover, it can be adapted to different ranges of accommodation.

10 The angliometer provides a comprehensive picture of both the horizontal and the vertical deviation in any measured position of gaze through the incorporation of lighted carriers that can be adjusted to correspond to ocular deviations for these different positions.

11 The fixational corneal light reflexes are additionally helpful in the objective study of (*a*) the near point of convergence, (*b*) the fixing, or dominant, eye, (*c*) primary versus secondary deviation, (*d*) ocular torticollis versus torticollis originating in the sternocleidomastoid muscle, (*e*) the range of monocular movements, (*f*) binocular fixation, (*g*) abnormal retinal correspondence, (*h*) true squint versus pseudosquint (angle gamma), and (*i*) amblyopia.

QUANTITATIVE COMPARISON OF METHODS OF ADMINISTERING PHYSOSTIGMINE

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Physostigmine, because of its potent parasympathomimetic action, has retained an important position in ophthalmic therapy since first used as a miotic by Laqueur (1876)¹ It is administered usually in an aqueous solution and less frequently in an ointment or lamella The official preparation is physostigmine salicylate, although the sulfate, which possesses similar pharmacologic properties, is also available

This paper presents a comparison of the effectiveness of the various methods of local application, including iontophoresis and the use of a wetting agent

In the selection of a method of administering a drug or in the adoption of a new method, its relative advantages and disadvantages must be carefully balanced As part of the evaluation it is desirable to know the amount of drug entering the eye Therefore a quantitative estimation was made of the physostigmine content of the aqueous humor of the rabbit's eye with different methods of application No local or general deleterious effects were noted with any of the procedures described A temporary corneal haze did, however, follow the iontophoretic experiments It disappeared in one-half hour to one hour No attempt was made to evaluate other factors, such as changes in vascularity, in tension and in the amount or content of the aqueous

PRELIMINARY STUDIES

No accurate quantitative test for the chemical analysis of small amounts of physostigmine could be found Biologic assay is the best method available Pulewka² introduced the white mouse pupil as a test object for atropine bioassay and demonstrated its advantages The superiority of the pupil of the white mouse over that of the cat was confirmed by Veit and Vogt³ and by Orzechowski and Hundrieser⁴ Von Sallmann⁵ used Pulewka's method for the estimation of atropine and scopolamine in different ocular structures Salt solutions of these drugs were introduced iontophoretically by various routes Investigation by Orzechowski and Hundrieser showed that the same method of bioassay was applicable to the quanti-

Supported by the Harriman Glaucoma Fund

From the Department of Ophthalmology, Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology, Presbyterian Hospital

1 Laqueur Ueber eine neue therapeutische Verwendung des Physostigmin, *Centralbl f d med Wissensch* **14** 421, 1876

2 Pulewka, P Das Auge der weissen Maus als pharmakologisches Testobjekt, *Arch f exper Path u Pharmakol* **168** 307, 1932, Ueber die Wertbestimmung von Heilmitteln, welche atropinartige Stoffe enthalten, *ibid* **180** 119, 1935

3 Veit, F, and Vogt, M Die Verteilung von Arneistoffen auf verschiedene Regionen des Zentralnervensystems, zugleich ein Beitrag zu ihrer quantitativen Mikrobestimmung im Gewebe, *Arch f exper Path u Pharmakol* **178** 534, 1935

4 Orzechowski, G, and Hundrieser, M Vergleichende Untersuchungen uber Genalkaloide und entsprechende Alkaloide, *Klin Wchnschr* **15** 481, 1930

5 von Sallmann, L Iontophoretic Introduction of Atropine and Scopolamine in the Rabbit Eye, *Arch Ophth* **29**:711 (May) 1943

tative estimation of physostigmine. It utilizes a series of white mice whose pupillary reactions have been standardized by the subcutaneous or intraperitoneal injection of known quantities of drug. The amount of physostigmine present in solutions of unknown concentration can then be determined by a comparison of the pupillary responses to the standards.

White mice weighing 16 to 22 Gm were used. The pupillary size was measured with a Leitz preparation microscope (ultrapaque) and ocular micrometer. A constant illumination was provided by a 6 volt tungsten bulb controlled by a rheostat and an ammeter in the electrical circuit. The minimum illumination that provided adequate visibility was chosen. The mouse pupil quickly assumed a stationary position that made possible an accurate measurement of the diameter.

The use of monochromatic light supplied by a red Wratten filter was tried in the hope of obtaining a light source that would not stimulate the rods of the mouse retina. A light source possessing this quality would give a larger pupil, increasing the range of contraction and therefore the accuracy of the test. At the beginning of an exposure red light did not appear to induce miosis, but a slow contraction followed, introducing a difficulty not compensated by its advantages, and its use was discontinued.

Readings were taken between 11 a. m. and 3 p. m. to avoid the physiologic morning and evening dilation. The mice were kept in a quiet, dark room a minimum of one-half hour before each reading. A measurement of the normal pupillary size was made preliminary to each test. Uncooperative or excitable mice and those with a pupillary variation greater than 0.05 mm from the average normal were not used. Animals were allowed a minimum of four days' rest between experiments.

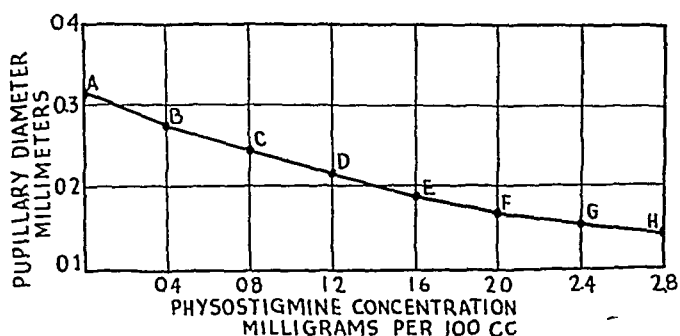


Chart 1—Standard curve showing the pupillary diameter of rabbits after injection of various amounts of physostigmine salicylate in 0.25 cc of distilled water. (A represents the pupillary diameter of a normal mouse which did not receive an injection, i. e. 0.31 mm.)

All solutions were used at room temperature. The injections were kept constant in quantity (0.25 cc) and were introduced subcutaneously. After the injection of test solutions, a three-quarter hour interval, corresponding to the time of the drug's maximal action, was allowed before determinations were made.

STANDARDS

A standard curve was prepared representing the effect of injections of 0.25 cc of distilled water containing respectively, 0.001 to 0.007 mg of physostigmine salicylate in gradients of 0.001 mg. All tests were repeated five times on groups of 5 mice each. The average normal pupillary diameter of each group measured 0.31 mm. Forty-five minutes later each pupil was again measured and the average for the 10 eyes determined.

The pupillary diameter produced by the injection of 0.001 mg of physostigmine salicylate equaled 0.27 mm. Similarly, the diameter produced by 0.002 mg equaled 0.24 mm, by 0.003 mg, 0.21 mm, by 0.004 mg, 0.19 mm, by 0.005 mg, 0.17 mm, by 0.006 mg, 0.15 mm, and by 0.007 mg, 0.14 mm. These results, plotted on a graph, are the basis for the standard curve illustrated in chart 1.

TECHNIC

Different methods of local administration of physostigmine were carried out on the eyes of albino rabbits. Each method was used five times. One hour after treatment 0.25 cc of aqueous humor was removed, with the eye under pontocaine anesthesia, with a hypodermic syringe fitted with a 27 gage needle. This was injected subcutaneously into a mouse. For each method a group of 5 mice with an average normal pupillary diameter of 0.31 mm was chosen. Forty-five minutes after injection the pupillary size of the mice was again measured and the average for the 10 eyes determined. The concentration of physostigmine was calculated by plotting the results against the standard curve, as shown in chart 2. In iontophoretic experiments a Birkhauser tube electrode⁶ was employed as the anode. The indifferent electrode was placed over the skull.

RESULTS

The administration of 0.1 cc of a 0.25 per cent commercial physostigmine salicylate ointment produced a concentration in the aqueous humor of 0.3 mg per hundred cubic centimeters.

One physostigmine salicylate ophthalmic lamella (0.11 mg) gave a concentration of 0.74 mg per hundred cubic centimeters.

One instillation of 2 drops (0.1 cc) of 0.5 per cent physostigmine salicylate in distilled water brought about a concentration in the aqueous humor too small to be determined accurately. However, when this amount was given twice with a ten

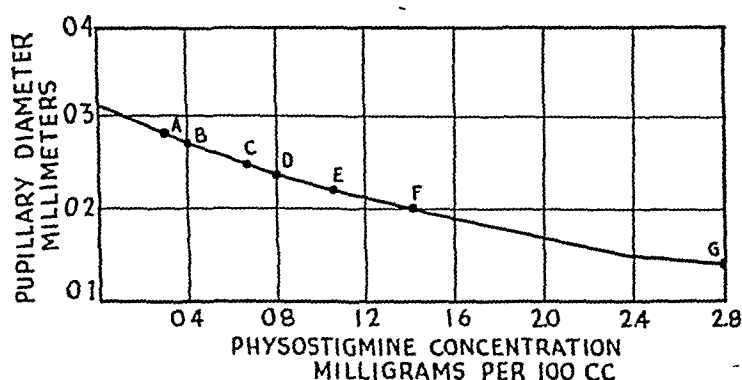


Chart 2—The pupillary diameter after A, 0.1 cc of a 0.25 per cent physostigmine salicylate ointment was applied, B, 0.1 cc of a 0.5 per cent solution of physostigmine salicylate in distilled water was instilled two times, C, one physostigmine salicylate lamella (0.11 mg) was applied, 0.1 cc of a 0.5 per cent solution of physostigmine salicylate in distilled water was instilled four times and iontophoresis with a 0.01 per cent solution of physostigmine salicylate in distilled water was carried out at 1 milliamperes for one minute, D, 0.1 cc of a 0.5 per cent solution of physostigmine salicylate in a 1:5,000 solution of zephiran and 0.1 cc of a 0.5 per cent solution of physostigmine sulfate in zephiran ophthalmic jelly were administered, E, 0.1 cc of a 0.5 per cent solution of physostigmine sulfate in a 1:5,000 solution of zephiran was instilled four times, F, iontophoresis with a 0.01 per cent solution of physostigmine salicylate in distilled water was carried out at 2 milliamperes for two minutes and iontophoresis with a 0.1 per cent solution of physostigmine salicylate in distilled water was carried out at 1 milliampere for one minute, and G, iontophoresis with a 0.1 per cent solution of physostigmine salicylate in distilled water was carried out at 2 milliamperes for two minutes.

minute interval, the concentration was 0.4 mg per hundred cubic centimeters. Four instillations at ten minute intervals resulted in a concentration of 0.68 mg.

The results obtained by O'Brien and Swan⁷ with carbamioylcholine chloride dissolved in a vehicle containing a surface tension-reducing agent stimulated a similar investigation with physostigmine. Physostigmine salicylate when dissolved

⁶ Birkhauser, R. Experimentelles und Klinisches zur iontophoretischen Behandlung von Hornhauttrübungen mit der Rohrenelektrode, *Klin Monatsbl f Augenh* 67:536, 1921.

⁷ O'Brien, C. S., and Swan, K. C. Carbamioylcholine Chloride in the Treatment of Glaucoma Simplex, *Arch Ophth* 27:253 (Feb) 1942.

in distilled water containing the same wetting agent zephiran⁸ in the same concentration, 1 5,000, yielded a cloudy precipitate. This wetting agent was found to be incompatible with salicylates. Substitution of the sulfate salt made a satisfactory mixture. This vehicle, when compared with distilled water alone, occasioned a significant increase in the concentration in the aqueous humor, a 2 drop instillation with a 0.5 per cent physostigmine sulfate solution producing a concentration of 0.8 mg per hundred cubic centimeters and four similar instillations, a concentration of 1.08 mg. All instillations were followed by gentle massage of the cornea through the lids.

The administration of 0.1 cc of a 0.5 per cent physostigmine sulfate solution in zephiran ophthalmic jelly produced a concentration of 0.76 mg per hundred cubic centimeters.

Iontophoresis employing a 0.1 per cent of physostigmine salicylate in distilled water and a current of 1 milliamperes for one minute resulted in a concentration of 1.46 mg per hundred cubic centimeters. When the amount of current and the length of time were both doubled, the concentration increased to 2.8 mg. A 0.01 per cent solution gave correspondingly lower concentrations, i. e., 1 milliamperes for one minute, a concentration of 0.62 mg, and 2 milliamperes for two minutes, 1.3 mg, per hundred cubic centimeters.

The addition of a wetting agent to the solutions used in iontophoresis did not increase their efficiency.

COMMENT

A general review of the literature advocating improved methods of ocular therapy in comparison with the standard form of instillation disclosed four main groups of agents: ointments or oily bases, ophthalmic disks or lamellas, solutions applied by iontophoresis and wetting agents. Quantitative bioassay of the aqueous humor of rabbits' eyes after administration of physostigmine with representatives of these four groups allowed the following deductions to be made:

In single treatments the ointment had a decided advantage over an aqueous solution. A lamella was twice as efficient as the ointment, and a surface tension-reducing solution or jelly corresponded in efficiency to the lamella. Iontophoresis was capable of producing concentrations three times as high as those produced by the lamella or the wetting agent.

The relative ease with which drops can be instilled warranted comparison of multiple instillations with iontophoresis. Application by means of an iontophoretic current of 1 milliamperes for one minute of a 0.01 per cent solution of physostigmine salicylate was approximately equal in efficiency to four instillations (2 drops every ten minutes) of a 0.5 per cent aqueous solution or one instillation of 0.5 per cent physostigmine sulfate in a surface tension-reducing solution. Four instillations of a surface tension-reducing solution were approximately twice as effective as four instillations of a simple aqueous solution, but not so efficient as iontophoresis with a 2 milliamperes current for two minutes and a 0.01 per cent solution or with a 1 milliamperes current for one minute and a 0.1 per cent solution. When the current was increased to 2 milliamperes for two minutes, iontophoresis with a 0.1 per cent solution was approximately two and a half times as efficient as repeated instillations of 0.5 per cent physostigmine sulfate in a wetting agent.

In acute congestive glaucoma and in preoperative high intraocular tension, when it is important to lower the tension quickly, physostigmine is most valuable. However, its intensive use has been limited by unpleasant systemic symptoms.

⁸ Zephiran is a mixture of high-molecular alkyl, dimethyl and benzyl ammonium chlorides.

The addition of a wetting agent increased the efficiency of the physostigmine drops, but there was an accompanying increase of absorption into the general circulation through the conjunctiva and, unless the lacrimal apparatus was compressed, through the mucosa of the lacrimal sac and the nose as well. Careful application of only sufficient solution to cover the cornea or use of a corneal bath technic would minimize undesirable absorption.

Iontophoresis employing a corneal tube electrode presented a method of obtaining greater concentrations of physostigmine in the aqueous humor with a negligible amount of systemic reaction. Before it can be recommended for treatment, however, its action on normal and pathologic intraocular tension will require further investigation.

CONCLUSIONS

- 1 Bioassay was applicable to the estimation of physostigmine in aqueous humor.
- 2 One tenth cubic centimeter of a 0.25 per cent physostigmine salicylate ointment when applied to a rabbit's eye gave a higher concentration in the aqueous humor than an instillation of 0.1 cc. of a 0.5 per cent solution in distilled water.
- 3 A lamella containing 0.11 mg. of physostigmine salicylate was twice as efficient as the ointment.
- 4 There was no appreciable difference between 0.1 cc. of 0.5 per cent physostigmine sulfate as a vehicle for a water-soluble jelly and a solution when each contained a wetting agent. The concentration in the aqueous humor produced approximated that produced by the lamella.
- 5 Iontophoresis employing a 2 milliampere current for two minutes and a 0.1 per cent aqueous solution of physostigmine salicylate increased the concentration over that obtained by a 0.1 cc. instillation of 0.5 per cent physostigmine sulfate in a surface tension-reducing vehicle by three and a half times.
- 6 Four instillations of a 0.5 per cent physostigmine sulfate solution containing a wetting agent gave a concentration twice that obtained by four instillations of a 0.5 per cent aqueous solution but less than half that obtained by iontophoresis with a 0.1 per cent aqueous solution and a current of 2 milliamperes for two minutes.

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Ophthalmologic Reviews

EDITED BY DR FRANCIS HEED ADLER

CLINICAL STUDY AND REVIEW OF TONOMETRY

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BROOKLYN

Several questions of interest arose in connection with tonometric measurements in the glaucoma clinic of the Long Island College Hospital (Dr Henry Mitchell Smith, director) Would it be possible, for instance, to determine whether the reliability of the measurements would be enhanced by use of the Schiøtz instrument or by use of the McLean instrument? Could a table of equivalents be arranged with which to check one instrument against the other, so that, given a reading with one instrument, one could with reasonable certainty judge the probable reading with the other? And, finally, was one instrument more reliable than the other when used on eyes with low tension, normal eyes and eyes with high tension?

A study of 205 eyes was made, without full knowledge of the work of other observers, in an effort to solve these questions It then seemed well to review the field of tonometry from Schiøtz' original contribution, in 1905,¹ which laid the groundwork and foundation for, and was actually the beginning of, modern tonometry This review consisted mainly of an evaluation of the Schiøtz and McLean tonometers

Much of this article will be elementary and some of it rather technical particularly in connection with Friedenwald's plan of study and the work of Harrington and Parsons, most of it will be a review, some of the details may be of historical interest, perhaps the content will prove to be somewhat informative by merely refreshing the reader's knowledge of the subject

It has been conceded, of course, that direct manometry is still the only scientifically accurate method of measuring the true intraocular pressure However, this method being clinically inapplicable, it was necessary to devise an instrument for estimating the intraocular pressure by interpretation of measurements taken of the impressibility of the globe

The development of the tonometer and the ingenuity exercised in its design are most interesting and have been ably reviewed by Lloyd² From the beginning there has been a constant striving for greater accuracy in the interpretation of the instrument's measure of ocular impressibility³

In 1868 Doi, in discussing one of the earliest models, gave expression to the following frequently repeated words, quoted by Lloyd² "The tonometer in its present form is as yet so far removed from exactness that it cannot be regarded as mathematically correct, but on the contrary it is sufficiently exact for both practical and clinical use"

From the Department of Ophthalmology, Long Island College of Medicine

Read at the staff conference of the Department of Ophthalmology, Long Island College Hospital, Oct 28, 1942

1 Schiøtz, H Ein neuer Tonometer, Arch f Augenh **52** 401, 1905

2 Lloyd, R I Tonometry and the Various Instruments Employed in Its Practice, Am J Ophth **13** 396 and 496, 1930

3 Harrington, D O, and Parsons, A H Tonometric Standardization, Tr Sect Ophth A M A, 1941, p 203

From that period to the present, approximately fifty different forms of tonometers have been devised, and within the last thirty years the form invented by Schiøtz has been the most generally used⁴ No doubt the ophthalmologist's requirements for clinical exactness have been greatly raised and he would no longer be satisfied with the crude model with which Dor worked Nevertheless, as pointed out by Friedenwald comparatively recently, there has been little exact knowledge as to what, precisely, one is measuring when one uses the tonometer, nor has it been known what interpretation to give to the divergent readings obtained with the different types of instruments

The first records of experiments in ophthalmomanometry were those of C. Weber in 1850, but he failed to draw any conclusions as to the normal intraocular tension Wahlfors in 1888, using a manometer in connection with a normal living human eye, found the intraocular pressure to be 26 mm of mercury The usual method of determining the intraocular pressure experimentally has been to introduce a cannula into the interior of the eye and attach a manometer by means of tubing to the cannula Both water and mercury have been employed in manometers, the choice depending on the construction of the apparatus Among the early experimenters were Weber, Leber, Neisnamoff, Pflüger, von Hippel, Gruhagen, von Schulten, Stocker, Starling, Adamuk, Holtske, Hill and Flack The experiments performed by these men were on dogs, rabbits and cats, and their conclusions were that the normal intraocular tension of these animals varies from 18 to 35 mm of mercury Weber and Wahlfors, according to McLean,⁵ experimented on the human eye

Before the days of the Schiøtz tonometer, estimations of pressure translated into millimeters of mercury were based on the experiment of Wahlfors His determination of 26 mm of mercury as the normal intraocular pressure was in harmony with the experiments on the lower animals made by other investigators This was the only experiment on record in which an eye of normal tension had been connected directly to a manometer When the Schiøtz tonometer was adopted, a new conception of the normal intraocular pressure was introduced⁵ With the advent of this instrument a point was reached at which the actual intraocular pressure of the average eye could be inferred with reasonable exactitude from a measure of its impressibility³

The original model of the Schiøtz instrument is well known The plunger is completely removable and has a concave surface at its point of corneal contact—continuous with the curve of the foot plate Separate weights of 5.5, 7.5, 10 or 15 Gm can be used as necessary, each being screwed, independently, on the center rod The amount of dimpling of the cornea is transmitted to the lever and shown on the scale By means of a graph or table the reading so obtained can be translated approximately into intraocular pressure in millimeters of mercury Schiøtz found that the results were most reliable when the readings were made as near as possible to figure 3 on the scale His original graph was based on readings obtained from the examination of 8 excised human eyes, each under eleven different manometric pressures, his findings at that time were that normal intraocular pressure varies from 15 to 25 mm of mercury

Schiøtz' experimental method, as described by Harrington and Parsons,³ was briefly as follows He connected the eye with a water manometer, and with a

⁴ Friedenwald, J. S. Contribution to the Theory and Practice of Tonometry, *Am. J. Ophth.* 20:985, 1937

⁵ McLean, W. Experimental Studies in Intra-Ocular Pressure and Tonometry, *Arch. Ophth.* 48:23, 1919

tonometer resting on the cornea measured the tonometer scale readings corresponding to different intraocular pressures. In each case two sets of readings were taken. First the connection between the eye and the manometer was left open. The pressure measured was the actual intraocular pressure with the tonometer in place. Second, the intraocular pressure was brought to a particular level, and the connection with the manometer was closed. The tonometer was then placed on the cornea and a reading made. Schiøtz used the results of the second method, which most closely approximates the clinical procedure in tonometry, to establish his nomogram, checking their accuracy by comparison with the results with the open manometer.

In 1915 Priestley Smith⁶ stated the principle of the ocular tonometer as follows:

The instrument measures the impressibility of the eyeball, and from the degree of impressibility we infer the intra-ocular pressure. The value of the inference is limited by the fact that the impressibility varies, not only with the intra-ocular pressure, but also with the size and structure of the eye.

He stated that in the early days of tonometry this limitation was clearly recognized, but that since the advent of the Schiøtz tonometer, which is more sensitive than any of its predecessors, it seemed to have been somewhat overlooked. He continued:

It has become customary to translate the readings into millimeters of mercury according to the chart of averages, and to quote the figures as though they correctly represented the intra-ocular pressure in the individual case. Professor Schiøtz, be it noted, has made no such claim for them. Even under the most favourable circumstances the tonometer cannot tell us the pressure with precision. Eyes which have the same pressure will sometimes give different readings, and eyes which have different pressures will give the same readings. This we know. It is inherent in the nature of the case. What we do not know is the amount of error which may arise.

Priestley Smith's experiments were made chiefly on human eyes *in situ* in dead subjects and on excised eyes of pigs, the latter being obtained immediately after death. A few were made, for comparison, on excised eyes of sheep and bullocks.

He stated that if all human eyes were alike in size and shape, and if their tunics were equally pliable and extensible, it might be possible to construct a scale according to which an accurate tonometric reading would tell the intraocular pressure with precision in every case. But as eyes differ in these respects, a scale which is used in all cases must be wrong in some, even if strictly correct for the average eye, it will fail for individual eyes.

Two separate questions arose for consideration in connection with Priestley Smith's experiments: 1. With what degree of accuracy can one measure the impressibility of the eye? 2. With what degree of accuracy does the impressibility indicate the intraocular pressure?

As for the first, he stated that by applying a tonometer several times in succession to a given eye, taking care that the same internal pressure is reestablished (experimentally) before each application, one can learn the degree of accuracy with which the instrument does its work, if the readings differ materially, either the mechanism of the instrument or the manner of using it must be faulty. He hastened to add that the workmanship of the Schiøtz tonometer was admirable and that frequently in his first trials he got variations amounting to two and even three divisions on the scale owing to incorrect placing of the instrument.

⁶ Smith, P. On the Limitations of the Tonometer, *Ophth Rev* 34 65, 1915

As for the second question—With what degree of accuracy does the impressibility indicate the intraocular pressure?—he stated that by applying the instrument to a number of different eyes in all of which the same internal pressure has been established, one can learn the extent to which the impressibility is influenced by conditions other than the height of the intraocular pressure. Accordingly, the amount of error likely to arise in a tonometric reading can be discovered by noting the extent to which the readings differ.

Priestley Smith concluded that

when a tonometric observation is recorded [with a Schiøtz instrument] it is the *reading* and not the *supposed equivalent* in mm Hg that should be stated [for instance, 3/5.5 Gm or 4/7.5 Gm]. The reading is a fact, the other is an inference which may be correct or incorrect.

Records in the form of mm Hg are undoubtedly attractive, for they give an impression of scientific accuracy, but they are really a source of confusion and lead to false conceptions.

We are told that the pressure in healthy eyes varies from 13 to 27 mm Hg. Whether this is true or not only the manometer could say for certain, but it is extremely improbable. It implies that not only the pressure of the intra-ocular fluid, but also that of the blood in the large veins of the retina and uveal tract, is twice as great in some eyes as in others, and all within healthy limits. Knowing as we do that the pressure in different eyes may seem to differ by 6 or 8 or even more mm Hg, while in reality it differs not at all, we may well doubt the inference in question.

Priestley Smith stated that if his own observations were correct, the Schiøtz chart would place the intraocular pressure several millimeters of mercury too low. It should be kept in mind that these observations were recorded in 1915 and that Priestley Smith was referring to Schiøtz' original graph.

Schiøtz himself advocated and set the example of recording readings and not supposed equivalents, and Elschmig,⁷ in thorough agreement, stated that pressure values in millimeters of mercury ought to be given only if the intraocular tension is exactly determined with a manometer.

Priestley Smith thoroughly supported the principle of the Schiøtz tonometer. He was careful to point out that his report was not an attack on this tonometer, but rather a defense of an admirable instrument against demands with which no instrument could possibly comply. He stated that the tonometer, though it cannot measure absolute pressure, can indicate changes of pressure with great precision. Applied to the same eye at different times, before and after an operation, before and after the use of a certain drug, at different hours of the day or night, and so forth, it can give invaluable aid in determining the occurrence of changes in pressure when these are doubtful. Again, as between the two eyes of the same person, when they are presumably alike in structure, it can be relied on to detect with certainty a difference of pressure much smaller than is discoverable by the finger.

When the eye of one person is compared with the eye of another or with a standard average, although considerable allowance must be made for the influence of structural differences, the tonometer is far more trustworthy than the finger as an index to the intraocular pressure.

In 1914 McLean⁸ introduced his direct reading tonometer, and in 1919⁵ he gave an account of his work to place tonometry on a more accurate scientific basis. The report included certain observations regarding the normal intraocular pressure.

All that McLean had set out to do was to improve or eliminate several features in the Schiøtz and Gradle tonometers. The Gradle tonometer was devised in

⁷ Elschmig, A. Designation of Tonometrically Ascertained Ocular Tension, *Klin Monatsbl f Augenh* 89 289, 1932, *Am J Ophth* 16 8, 1933.

⁸ McLean, W. Preliminary Report of a New Tonometer, *J Ophth, Otol & Laryng* 20 432, 1914.

1911⁹ It is essentially the Schiøtz instrument with several modifications. It is constructed more firmly, the handles are circular where grasped between the fingers, the corneal foot plate and stylet are smaller, the stylet is so attached that it cannot be dropped out of the tube in which it slides, and the four weights are each 1 Gm being added to one another when the resistance of the hardened eyeball makes a heavier weight necessary. Every third marking on the recording scale is numbered in order to facilitate the tonometric reading. A chart is furnished which translates the tonometric readings into millimeters of mercury according to the empiric standard adopted by Schiøtz.

There were several respects in which McLean thought that the Schiøtz tonometer could be improved on. His criticisms were that (1) the reading scale of the instrument is too far away from the eye under examination, (2) the necessary translation of the reading into millimeters of mercury is cumbersome (3) the chart supplied is a trying one to decipher, (4) the method of changing weights is difficult and time consuming and (5) the plunger fits the foot barrel so closely that capillary attraction may impair the accuracy of the reading.

The McLean instrument differs in many ways from those previously presented. The arc of the indicating needle is below instead of above, as in the Schiøtz and Gradle models, so that the numbered reading scale is as close as possible to the eye under examination. The scale is graduated in millimeters of mercurial pressure from 10 to 130, making possible a direct reading of the intraocular pressure, without recourse to graphs, and eliminating the need for noting millimeter or fractional millimeter oscillations. No weights are needed. The plunger is so supported that "no drag is produced by the capillary attraction of any fluid which may have remained on the cornea at the time of placing the instrument for a reading."

Several years were spent by McLean in experimentation to overcome mechanical difficulties before all was in readiness for the scale and the determination of the pressure according to the manometer. It was while attempting to check the accuracy of a testing apparatus with a Schiøtz tonometer that McLean discovered that the tonometer did not agree, neither did several other Schiøtz tonometers or a Gradle instrument. These tonometers gave lower readings than the manometer. It was then that experiments were conducted to investigate further the matter of normal intraocular pressure.

McLean's experimental results tended to revert to the standards established by Wahlfors and the early experimenters rather than the newer scale of the Schiøtz tonometer. They were performed on rabbits and dogs and on 3 living human eyes *in situ*. The 3 living eyes were all glaucomatous and were being removed on account of uncontrollable pain. The experiments on 2 were performed before McLean's tonometer was perfected. For the first eye, the measurements were 50 with the Schiøtz tonometer and 65 with the manometer. Tests made after enucleation disclosed the same variation. For the second eye, the measurement was 72 with the Schiøtz tonometer and 88 with the manometer. For the third, on which both tonometers were used, the Schiøtz instrument gave a measurement of 40, the McLean of 58 and the manometer of 60.

The present scale on the McLean tonometer was adopted on the basis of tests of nearly 200 enucleated eyes and a considerable number of eyes *in situ* of the lower animals. With this tonometer, the lower limit of normal intraocular pressure is to be considered as 22 and its upper limit not above 40. McLean stated that it is difficult to give an absolute limit of normal tension.

9 Gradle, H. Modification of Schiøtz Tonometer, *Ophth Rec* 20:19, 1911.

McLean¹⁰ had joined Weber and Wahlfors and Wessely and Seidel as one of the only men who had done any experimental work on living human eyes by connecting the interior of the eye to a manometer.

During the course of the experiments on rabbits, an apparently new observation was made, namely, that the tonometer disclosed a marked difference in intraocular pressure with the eye under local and under general anesthesia. This was borne out by manometric readings, the tension dropping anywhere from 3 to 11 mm during general anesthesia.

In all the experiments⁵ on the living eye, both human and animal, the intraocular pressure was highest during local anesthesia, and as soon as the subject was thoroughly under the influence of ether, the pressure was lowered, the deeper the anesthesia, the lower the pressure, until a limit was reached. In animals it was noted that the pressure rose after the ether cone was removed, so that it was back to its original level as the animal regained consciousness. In the first of the cases of enucleation, the Schiøtz tension of the glaucomatous eye dropped from 75 under local anesthesia to 45 and that of the healthy eye from 19 to 10. In the second case, the tension of the glaucomatous eye dropped from 88 under local to 72 at the first reading under general anesthesia and to 47 as the anesthesia was increased.

Schiøtz' reply to McLean's criticisms of his instrument was as follows: 1. The distance between the reading scale and the eye matters but little. 2. Tonometric readings cannot be accurately translated into intraocular pressure in millimeters of mercury and it is preferable to state the weight used and the reading obtained, in the form of a fraction or otherwise, and to follow this with a figure designating the pressure deduced. McLean short-cut the calculations and arrived directly at the deduced pressure. 3. The chart can easily be enlarged. 4. It is a disadvantage to employ a constant weight, as in the McLean instrument, much more reliable indications are obtained by varying the weight according to the needs in the individual case. Schiøtz defended this thesis in considerable detail. 5. As to the influence of capillary action, he expressed the opinion that this factor is negligible, Elliot¹¹ agreed, stating that he had strong practical reasons for believing this opinion to be correct. Elliot's opinion, after using both instruments, was that the low position of the McLean scale is a distinct advance.

Dr. Marple, who claimed the distinction of bringing the first Schiøtz tonometer into this country, had become greatly interested and had been present at many of McLean's experiments. He requested the privilege of sending Dr. Schiøtz one of McLean's tonometers together with a diagram of the testing apparatus and the results of the tests he had seen. He desired Dr. Schiøtz' criticism of the apparatus and some explanation of why the results did not agree. In his reply, quoted by McLean,¹⁰ Schiøtz failed to criticize the apparatus and the method of the testing, and his only comment relative to the experiments was, "Dr. McLean evidently has values different from mine. I do not understand why."

In 1920 Schiøtz¹² wrote that, although during the years since he had introduced his instrument he had never ceased to occupy himself with the tonometer, it had not been until the previous three or four years that he had been able to turn his full attention to a close investigation of the subject. His aim was partly to improve the instrument if possible, partly to extend existing knowledge of the mode of action

10 McLean, W. Development of a Tonometer, *Am J Ophth* 2 417, 1919.

11 Elliot, R. H. A Treatise on Glaucoma, ed 2, New York, Oxford University Press, 1922.

12 Schiøtz, H. Tonometry, *Brit J Ophth* 4 201 and 249, 1920.

of the tonometer and partly to check and correct the curves the construction of which had been based on not more than 8 enucleated eyes

Schiøtz conceded that, as might have been expected, the graphs based on measurements of 8 enucleated eyes were incorrect, and in 1924, utilizing the measurements of Priestley Smith on 12 dead eyes *in situ* and additional data he himself had obtained during the previous year on 30 dead eyes *in situ*, he compiled a new graph, which showed the readings in mercurial pressure to be 4 mm higher than the computations on the graph accompanying the original instrument. Of the 30 eyes experimented on, 20 were in persons who had been dead for from eight to forty-eight hours prior to the measuring, on the remaining 10 the measurements were made one to two hours after death. Several measurements were taken for each pressure height. Schiøtz found no important difference between the two groups regarding the deflections, and he concluded that one may safely assume that for each degree of pressure the maximum and minimum deflections in living eyes will be about the same as in dead eyes. For these measurements Schiøtz used his old standard tonometer, which had been used for all his previous measurements and as the standard for the adjustment of other tonometers.

A deflection of 3 mm (5.5 Gm in weight) is the approximate limit for the normal intraocular pressure, and its mercury value is about 4 mm higher than originally assumed. Schiøtz stressed the fact that to investigators who have recorded the deflections as the measure of the intraocular pressure, which is really the only correct method, the changes in mercury values are of no importance, because at present, as before, deflections of between 3 and 6 mm or more signify the normal intraocular pressure. Those who have translated the deflection values into millimeters of mercury must rectify these according to the new graphs.

At the time that Schiøtz compiled his new graphs (in 1924),¹³ he again emphasized the fact that a given deflection does not indicate a definite pressure in millimeters of mercury, that it represents a range between the maximum and minimum which is not insignificant. If, he stated, one fixes a deflection of 3 mm (5.5 Gm weight) as the limit between the normal and pathologic pressure, one does so because it represents a range between the normal and the pathologic. The boundary is never sharply defined. Consequently, with a deflection of 3 mm (5.5 Gm) the pressure will as a rule be about 29 mm of mercury, but that deflection might be properly referable to the minimum graph and to an intraocular pressure of 26 mm or to the maximum graph and a pressure of 33 mm. In other words, the deflection of the pointer does not indicate a precise pressure but a pressure *range*, which for the 5.5 Gm weight is about 6 to 8 mm, for the 7.5 Gm weight 8 to 10 mm, for the 10 Gm weight about 13 mm and for the 15 Gm weight about 15 mm. Nor can it be otherwise, continued Schiøtz, when one takes into consideration the individual peculiarities in the size of the eyes and in the thickness and elasticity of their walls.

Priestley Smith's comment summarized the status of tonometry at the time: "We have here the limitation of the tonometer, and the fact cannot be altered as long as we employ the principle in question." Schiøtz¹² stated that he could not imagine any method available for living eyes by which the errors due to variations of the envelope could be eliminated.

In connection with this consideration of the variables in tonometry, Elliot¹¹ in 1922 wrote that there had been apparently unanimous recognition, by investigators who had carefully worked on the subject, of the profound influence, at least

13 Schiøtz, H. Tonometry, *Brit. J. Ophth* 9 145, 1925

theoretic, of the rigidity or elasticity of the tunic of the globe and of differences in the radius of curvature on the tonometric determinations. Where the authorities differ, he stated

is in the matter of the extent to which this factor influences the readings obtained. Some observers think it to be of such great importance that it invalidates their scientific accuracy. McLean, on the other hand, whose admirable work on a large number of living eyes entitles his opinion to the greatest respect, does not agree with this assumption, and believes that, provided we have to do with a living eye, the overwhelming factor in the determination of the tonometer reading is the intra-ocular pressure, the condition of the tunic being comparatively unimportant. Obviously gross pathological change, such as calcification of the tunic, is excluded.

After working on the problem for a considerable time, Schiøtz constructed a new model of his instrument, presented in 1924,¹² in which the plunger and weight form one piece, which may be put into the cylinder from above. If a heavier weight is needed, another weight may be placed on top of the first one. This improvement eliminates the criticism often directed to the difficulty encountered in screwing on and off different weights for higher pressures. According to Schiøtz, the sliding cylinder with the small round disks has been replaced by one with ball bearings, making the cylinder more solid and the tonometer better balanced. In principle, however, the old model was retained.

During the course of his experiments, Schiøtz became aware of the extraordinary influence of the shape of the lower end of the plunger on the extent of the deflections of the pointer. This detail is elaborated on here because of several references that will be made subsequently. In the Schiøtz tonometer, the lower end of the plunger is concave, and the radius of curvature is the same as that of the concave surface of the base, viz., 15 mm. For technical reasons, the question was raised as to whether the lower end of the plunger should be made flat. Schiøtz recorded certain measurements obtained, respectively, with plungers having the ordinary concave end surface, a plane surface and a convex surface. They showed a surprising difference in the deflections of the pointer, especially as between the concave and the convex surface. This great difference, Schiøtz stated, was surprising but the explanation simple. In each case the plunger sinks into the membrane and depresses it until the depressed area is supported from below by a pressure that balances the weight of the plunger and its controlling parts, in each case the "supporting area" is the same but to obtain it the convex plunger must sink more deeply than the concave.

With a convex plunger and a relatively small weight one can deal with a large range of pressures, and Schiøtz stated in his earlier work that he ought perhaps to substitute a convex plunger for the concave in order to avoid the troublesome addition and removal of weights and the need for the corresponding four curves. On the other hand, he feared that the relatively small intervals between the deflections with the convex plunger in the case of high pressure would make the measurements less trustworthy and would result in objections to the proposed change.

However, Schiøtz was not inclined to abandon the idea of the convex plunger, for further experiments showed that just in the region with which one is most concerned the deflections are not smaller but considerably larger than with the concave. Additional studies were undertaken with the convex plunger in order to find the weight most suitable for clinical use, 52 Gm for the plunger and its belongings was determined as the best. This weight gave a sufficiently large range, namely, from 22 mm of mercury (deflection, 5.6 mm) to 90 mm (deflec-

tion, 0) And so, in 1927, Schiøtz introduced a tonometer with a convex plunger, which he named the Schiøtz x-tonometer¹⁴

When comparative measurements with the two instruments were made on the same eye, Schiøtz found the readings equally constant with each, but when they were made on a number of different eyes it was noticeable that in cases in which the concave plunger gave uniform readings, the convex often showed slight variations which could hardly be attributed to error. He stated the belief that the small discrepancies were due to slight differences in the thickness and elasticity of the corneas, so small that the flatter surface of the concave plunger is not influenced by them, while the convex plunger, which sinks deeper and is more closely surrounded by the cornea, is sensitive to them. The flat plunger he believed to be undesirable because a slight error toward either convexity or concavity causes perceptible variations in the deflections.

After a thorough consideration of the question, Schiøtz concluded that for the time being at least it would be preferable to retain the plunger with the concave surface. He said¹⁴

This tonometer has now been tried for many years and has shown itself—*when correctly standardized*—to be a practical instrument for clinical use. The earlier disadvantage of having to screw the additional weights on and off is done away with, for the original weight of 55 gm. can now be added to by simply laying on it the 75 gm., 10 gm., or 15 gm. weight.

I must add, however, that the x-tonometer also is a good instrument, it gives a constant deflection and unquestionably it is safer for the corneal epithelium, especially in eyes with high pressure for which with the concave plunger one must use a proportionately high weight. Whatever shape be adopted, it is clear that the deflections given by different tonometers will not be comparable if the plungers are differently shaped.

The weight of the Schiøtz tonometer is represented by two distinct parts acting independently. The one consists of the cylinder, with its cup-shaped base, together with the loop carrying the flat strip and the graduated arc. This part of the tonometer weighs 10.1 Gm.¹² The other part consists of the plunger, with its loose weight, together with the pointer. The weight of this part varies with the loose weight employed. It is 55, 75, 10 or 15 Gm., respectively.

Schiøtz stated that the use of loose weights which have to be changed during the examination may appear inexpedient. Certainly it would be easier to use only one, but this would have to be considerably larger, an innovation which he considers absolutely wrong. A heavy weight means an unnecessary strain on normal eyes and causes a depression in the cornea of 1 mm. or more, which, Schiøtz wrote, is undesirable and according to his experience will not increase the reliability of the indications. His opinion is that the most reliable deflections are those from 1 to 5 mm. or, at most, 10 mm. If a deflection smaller than 1 mm. is obtained, a heavier weight should be employed, and if with a heavier weight the deflection is greater than 5 to 6 mm., a lighter weight should be substituted.

Schiøtz' declared that a heavy weight does not give exact information with regard to eyes with normal or slightly increased pressure, it causes fluid to be pressed out of the eye and thus reduces the pressure below its original state. He said that experimental measurements show that it is inadvisable to use weights that are heavier than is absolutely necessary for the production of reliable deflections of the pointer.

¹⁴ Schiøtz, H. Tonometry. A Tonometer with Convex Plunger, Brit J Ophth 11 116, 1927

In this connection, it is interesting to note a report by Bock, Kronfeld and Stough,¹⁵ that

The behavior of the intra-ocular tension of normal eyes in response to the application for two minutes of a [Schiotz] tonometer carrying a 15 Gm weight was studied on fifty persons. In every case the tension dropped in proportion to the original tension. Normal eyes with tensions between 27 and 32 mm showed a greater decrease than a small number of glaucomatous eyes with the same original tensions.

Friedenwald has stated that the actual expulsion of fluid from the ocular cavity cannot be instantaneous and may be reduced to a minimum by a reduction in the time of the tonometric reading to as short a period as possible.

In commenting on two tonometers made in America, Schiøtz¹² stated that the Gadde instrument is the Schiøtz tonometer except for a few "improvements" and that the McLean tonometer is

a very beautiful instrument, but, to tell the truth, I cannot in this case either find any real difference between it and the Schiøtz. The design and the principle are similar, though the index is made to point downwards instead of upwards. A few other slight alterations have been made, and these undoubtedly will influence the measurements, so that it will probably give results a little different from those obtained by the Schiøtz tonometer.

McLean's tonometer subjects all eyes to the pressure of a considerable weight, viz. 25 grm, of which 12-15 grm falls on the plunger. For most eyes this weight is unnecessarily heavy, more than 10 grm being needed only in very rare cases. For reasons already given I consider it undesirable to graduate the scale in mm Hg, as in the McLean tonometer.

That Dr. McLean found the values obtained with the McLean and Schiøtz tonometers to differ considerably is due, I think, in the first place to the fact that the Hg values for the Schiøtz were too low, and, secondly, in some degree, to differences in the relative weights of the various parts of the instruments and other differences. The tonometer is a very sensitive instrument, and the slightest alteration in any detail is likely to influence the deflections. For example, I have learnt recently that the lower end of the plunger in the McLean tonometer is convex.¹⁶ I have already shown that the shape of the plunger has an important influence on the deflections.

The values [with the Schiøtz and the McLean tonometer] can hardly be compared for they lie differently on the scale, but the instrument does not appear to offer any real improvement as regards reliability of measurement. The McLean tonometer is a Schiøtz tonometer partly turned upside down, and as it is similar to the older instrument both in principle and build, it should measure as well, but nothing has been added which could lead us to expect it to measure better.

Schiøtz expressed his gratitude to Priestley Smith for his exposition of the Schiøtz tonometer and stated that he fully agreed with his conclusion that "It is not proved, and it is not likely, that the instrument errs to the extent that McLean's experiments suggest."

Elliot commented on Schiøtz' criticism of the McLean instrument on the ground of its high fixed weight and stated that McLean's experiments on living human eyes would seem to show that it is an accurate instrument when used on eyes with high pressure, whatever it may be on normal ones, and he added that clinical experience with the instrument serves to prove that its indications with regard to normal eyes can safely be relied on, for they are consistent with the other features present.

Elliot has used both the Schiøtz and the McLean tonometer, and he has expressed his confidence that either will prove invaluable to the surgeon who accustoms himself to its use.

15 Bock, J., Kronfeld, P. C., and Stough, J. T. Effect on Intra-Ocular Tension of Corneal Massage with the Tonometer of Schiøtz, *Arch. Ophth.* **11** 797 (May) 1934.

16 In a personal communication to the author, Dr. McLean wrote that the lower end of the plunger of his tonometer is flat.

TABLE 1—*A Comparison of Pressure Readings Obtained with the Schiøtz and the McLean Tonometer (Millimeters of Mercury)*

Schiøtz Tonometer (Original Model)			Schiøtz Tonometer (Original Model)		
Original Graph	1924 Graph	McLean Tonometer	Original Graph	1924 Graph	McLean Tonometer
7	10	12	19	23	29
8	11	17	19	23	29
10	13	12	19	23	30
10	13	15	19	23	30
10	13	16	19	23	30
10	13	16	19	23	30
10	13	18	19	23	32
10	13	19			
10	13	20	20	24	23
			20	24	28
11	14 5	15	20	24	28
11	14 5	20	20	24	30
12	15 5	15			
12	15 5	15	20 5	24 5	29
12	15 5	16	20 5	24 5	29
12	15 5	16	20 5	24 5	29
12	15 5	18	20 5	24 5	30
12	15 5	18	20 5	24 5	30
12	15 5	18	20 5	24 5	30
12	15 5	18	20 5	24 5	31
12	15 5	18	20 5	24 5	31
12	15 5	19	20 5	24 5	32
12	15 5	19	20 5	24 5	32
12	15 5	19	20 5	24 5	32
12	15 5	20			
12	15 5	22	21	25	32
12	15 5	25			
			22	26	28
12 5	16 5	16	22	26	28
12 5	16 5	18	22	26	30
12 5	16 5	18	22	26	30
			22	26	30
13	17 5	18	22	26	31
13	17 5	19	22	26	31
13	17 5	19	22	26	31
13	17 5	20	22	26	31
13	17 5	22	22	26	31
13	17 5	23	22	26	32
13	17 5	23	22	26	32
13	17 5	23	22	26	32
13	17 5	25	22	26	33
			22	26	33
14 5	19	19	22	26	33
14 5	19	22	22	26	33 5
14 5	19	23	22	26	34
14 5	19	24	22	26	34
14 5	19	25	22	26	35
14 5	19	28	22	26	35
			22	26	35
16	20	21	22	26	35
16	20	22	22	26	35
16	20	23	22	26	36
16	20	26	22	26	36
16	20	26			
16	20	26	23	27	33
16	20	26	23	27	35
16	20	26			
16	20	26	24	28 5	32
16	20	26	24	28 5	32
16	20	27	24	28 5	32
16	20	27	24	28 5	35
16	20	27	24	28 5	35
16	20	28	24	28 5	35
16	20	28	24	28 5	36
16	20	28	24	28 5	37
			24	28 5	38
17	21	27	24	28 5	39
17	21	27			
			26	31	32
17 5	21 5	25	26	31	32
17 5	21 5	26	26	31	32
17 5	21 5	27	26	31	34
17 5	21 5	29	26	31	36
			26	31	36
18	22	24	26	31	36
18	22	27	26	31	36
18	22	28	26	31	36
			26	31	38
19	23	25	26	31	40
19	23	25	26	31	42
19	23	27	26	31	43
19	23	27			
19	23	27	28	32 5	40
19	23	27	28	32 5	40
19	23	27			
19	23	28 5	28 5	33	35
19	23	29	28 5	33	36
19	23	29	28 5	33	37
19	23	29	28 5	33	38

TABLE 1—*A Comparison of Pressure Readings Obtained with the Schiøtz and the McLean Tonometer (Millimeters of Mercury)—(Continued)*

Schiøtz Tonometer (Original Model)			Schiøtz Tonometer (Original Model)		
Original Graph	1924 Graph	McLean Tonometer	Original Graph	1924 Graph	McLean Tonometer
28 5	33	39	40	45	53
28 5	33	39			
28 5	33	40	42	46	50
28 5	33	41	42	46	55
28 5	33	42	42	46	56
28 5	33	43	42	46	57
			42	46	60
29	33 5	38	42	46	62
29	33 5	40	42	46	63
31	35 5	34	43	47	55
31	35 5	40			
31	35 5	40	46	51	60
31	35 5	40	46	51	61
31	35 5	40	46	51	62
31	35 5	41			
31	35 5	42	50	54	65
31	35 5	43	50	54	70
33	37 5	48	56	60	65
33 5	38	45	60	64 5	98
33 5	38	50	60	64 5	105
34	39	39	65	69 5	90
			65	69 5	95
36	41	50			
39	44	53	70	75	80
39	44	55	70	75	85
39	44	55			
39	44	55	89		110

In summarizing his thoughts in regard to the choice of an instrument, James W. Smith¹⁷ stated that every ophthalmologist who employs a standard tonometer has learned to know from experience what the normal reading is for his instrument and what constitutes an increase or decrease. He stated the belief that the controversy regarding the calibration of some instruments as compared with actual readings of intraocular pressure obtained with a manometer is chiefly of scientific and academic concern. It has been generally accepted that the relative readings of tonometry are of much greater practical importance than the absolute ones.

In 1932 Shope¹⁸ undertook a study in tonometric measurements in a large series of cases in an effort to obviate the confusion resulting from the multiplicity of tonometers in general use and the interpretation of their readings. The purpose of this clinical investigation was to compile a table of comparative values for three popular tonometers, namely, the Schiøtz, the McLean and the Baillart, giving a sufficient number of values to be practical, based on the application of the tonometer to human eyes.

The Baillart tonometer was included in the study because, according to Shope, "This tonometer, because of its several new and practical features, has bid for a place in the ophthalmologist's armamentarium. These features include the direct reading in millimeters of mercury, no weights to change, and applicability in the erect posture and upon the sclera." Baillart stated that his tonometer had been standardized with the Schiøtz instrument and adjusted to read the same, and it therefore seemed advisable to determine whether these two tonometers did read the same when applied to the same eyes.

Approximately 10,000 tonometric readings were taken for Shope's study. Of these, 1,687, taken on 220 eyes, were selected for further consideration. The others were rejected because the application of tonometers lowered the intraocular pressure, making parallel readings impossible.

17. Smith, J. W. Tonometry, *Am J Ophth* 9 773, 1926

18. Shope, P. A Study in Tonometric Measurements, *Am J Ophth* 15 739, 1932

A reading with a Schiøtz tonometer was obtained before and after each series of tension readings. Only those series were considered in which these two readings were the same or there was a reduction in tension not greater than one division on the Schiøtz scale.

The corneal curvature was determined in all cases with an ophthalmometer. No eyes were studied further which showed irregularities, an unusually high or low curvature or a large amount of astigmatism of the anterior surface of the cornea.

Although it was found that most eyes became softer after a tonometer was applied to the cornea a few times, many normal eyes, with a tension of 17 to 22 mm of mercury (Schiøtz), did not become altered in intraocular tension by several applications of various tonometers. Many glaucomatous eyes became softer after a tonometer was applied a few times. The tension became less in practically all eyes after the McLean tonometer was applied two to four times. Priestley Smith has stated that the eye becomes softer after application of a tonometer by expression of fluid from the anterior chamber and that absence of this softening is a nearly constant indication of obstructive changes in the filtration angle. On the basis of his own observations, Shope concluded that apparently some factor other than the patency of the filtration angle must play a role in the softening.

In this study it was found that five Schiøtz tonometers, all in good repair, gave different readings when applied to the same eyes. Three of these were manufactured in Norway. Two were certified. The other two were of German manufacture. The readings with these tonometers occasionally differed as much as 15 mm of mercury on an eye of normal intraocular tension and 15 to 20 mm on a glaucomatous eye. Exact agreement was unusual.

With two Schiøtz tonometers and two McLean tonometers, a comparative study was made and tabulated. It was found that the equivalent values for these two kinds of tonometers were about as given by McLean and Schiøtz on the average but for any given Schiøtz reading there was a considerable range in McLean readings.

Shope concluded that there is no exact parallel between readings obtained with the Schiøtz and with the McLean tonometer. For example, the McLean instrument gave a reading of 36 mm for an eye for which the reading was 22 mm with the Schiøtz tonometer, for another eye the values were 36 mm with the McLean and 33 mm with the Schiøtz instrument. For another eye the readings were 41 mm with the McLean and 27.5 mm with the Schiøtz, while still another eye registered 41 mm with the McLean and 36 mm with the Schiøtz tonometer.

Since a wide range of equivalents with one tonometer was found for any given reading with the other, no chart of exact or nearly exact equivalents could be drawn up, and only such a chart could have much practical value.

A series of tension readings was taken in which the Schiøtz and the Baillart tonometer were compared. On the average, the Baillart tonometer agreed fairly closely with the Schiøtz, the usual variation being 3 to 5 mm of mercury. Occasionally large differences between the two were encountered, 1 eye registered 35 mm with the Schiøtz and 16 mm with the Baillart.

Readings obtained with the Baillart tonometer applied to the cornea with the patient erect and with the patient recumbent agreed or differed less than 3 mm in 75 per cent of cases. Scleral readings with the Baillart instrument were often surprisingly accurate, but just as often surprisingly inaccurate.

In the series reported on in the present paper, 410 measurements were taken on 205 eyes. One Schiøtz and one McLean tonometer were used. The Schiøtz

instrument was an original model of Norwegian manufacture. It has served me well for many years, and I have considered it reliable in its indications. Both instruments recorded properly when placed on their respective testing surfaces. In several instances the Schiøtz instrument was checked with a similar model of similar manufacture belonging to Dr. Henry Mitchell Smith, and on those occasions both instruments recorded alike or with negligible variation.

Corneal curvature was not measured, but no eyes were included that showed extensive corneal scarring. A tonometric measurement was taken with the Schiøtz instrument first, and this was followed by a reading with the McLean tonometer after one minute. All readings were taken by me.

As will be noted in table 1, for practically every reading with the Schiøtz instrument there was a range of readings with the McLean. For instance, 16 eyes that measured 20 mm of mercury Schiøtz (1924 graph) gave readings of from 21 to 28 mm McLean. Twenty-five eyes measured 26 mm Schiøtz and 28 to 36 mm

TABLE 2—*Summary of Pressure Readings Obtained with the Schiøtz and the McLean Tonometer (Millimeters of Mercury)*

Number of Eyes	Schiøtz Tonometer			Number of Eyes	Schiøtz Tonometer		
	Original Graph	1924 Graph	McLean Tonometer		Original Graph	1924 Graph	McLean Tonometer
1	7	10	12	10	28.5	33	35-43
1	8	11	17	2	29	33.5	38-40
7	10	13	12-20	8	31	35.5	34-43
2	11	14.5	15-20	1	33	37.5	48
15	12	15.5	15-25	2	33.5	38	45-50
3	12.5	16.5	16-18	1	34	38	39
8	13	17.5	18-25	1	36	41	50
6	14.5	19	19-28	4	39	44	53-55
16	16	20	21-28	1	40	45	53
2	17	21	27	7	42	46	50-63
4	17.5	21.5	25-29	1	43	47	55
3	18	22	24-28	3	46	51	60-62
18	19	23	25-32	2	50	54	65-70
4	20	24	23-30	1	56	60	65
11	20.5	24.5	29-33	2	60	64.5	98-105
1	21	25	32	2	65	69.5	90-95
25	22	26	28-36	2	70	75	80-85
2	23	27	33-35	1	89		110
10	24	28.5	32-39				
13	26	31	32-43				
2	28	32.5	40				
				205			

McLean. Seven eyes that measured 46 mm Schiøtz gave readings of from 50 to 63 mm McLean. There were similar ranges of values in practically all the other groups. Conversely, for practically every reading with the McLean instrument, there was a range of readings with the Schiøtz.

The readings on this series of eyes tend to show that the equivalent values of the two tonometers are about as given by McLean and Schiøtz. For instance, 18 eyes that measured 23 mm of mercury Schiøtz (1924 graph) showed an equivalent of 25 to 32 mm McLean (table 2). This is well within the average normal for both instruments. Twenty-five eyes that measured 26 mm Schiøtz showed an equivalent of 28 to 36 mm McLean. This is still within the normal range. Ten eyes measured 28.5 mm Schiøtz, with an equivalent of 32 to 39 mm McLean. At this point one begins to reach the approximate upper limits of normal for both instruments. Thirteen eyes measured 31 mm Schiøtz and 32 to 43 mm McLean, and 10 eyes measured 33 mm Schiøtz and 35 to 43 mm McLean. The last 2 Schiøtz readings, 31 and 33, are somewhat above the upper limit of normal 29 mm, and, similarly, the McLean readings have passed the recognized upper

limit of normal, 40 mm. As one gets to the higher Schiøtz readings, the McLean equivalents are also definitely above normal. One eye measured 39 mm with both instruments.

On the basis of this data, one can only subscribe to the conclusions reached by Shope in his study.

Shope called attention to the tenet already recognized almost unanimously as fundamental, that no tonometer may be expected to give a definite idea of intraocular pressure until the variables which enter into tonometry can be controlled or calculated. He listed the principal variables as follows: (1) impressibility of the cornea, (2) distensibility of the corneoscleral coat, (3) compressibility of the choroid, (4) freedom of outflow of the aqueous, (5) amount and compressibility of the orbital fat, (6) corneal curvature and (7) size of the globe, as, other things being equal, a large globe will distend more than a small one.

Harrington and Parsons have more recently regrouped into the following classification the factors which, aside from the actual intraocular pressure, determine a tonometric reading: (1) rigidity of the ocular coats, (2) volume of corneal indentation produced by the tonometer plunger, (3) distortion of the cornea by the tonometer foot plate irrespective of indentation by the plunger, (4) expulsion of intraocular fluid by the weight and by the manner of application of the tonometer and (5) mechanical accuracy of the tonometer as to (a) adherence to specifications and (b) reduction of reading errors.

Shope also called attention to several possible causes of error that may decidedly influence the accuracy of a tonometric reading. It might be well to keep them in mind: (1) tonometer not applied to the corneal center, (2) tonometer not erect, (3) fingers pressing on the globe, (4) lids touching the cup-shaped base, (5) patient squeezing the eyelids, (6) unsteadiness of fixation of the eye, (7) lack of correction for movements of the eye when it is covered, the movements being due to heterophoria, and (8) pressing down or lifting up on the handle of the Schiøtz or McLean tonometer (this is regulated on the Baillart instrument).

In 1936 Adler, Berner and Meyer¹⁹ reported the results of a comparison of tonometers for their clinical accuracy. They devised an instrument for the testing and compared the readings of different tonometers with actual intraocular pressures and the readings of standard tonometers of the same make at different pressures. Schiøtz, McLean and Gradle tonometers were found to be sufficiently accurate for clinical purposes. Between the pressures of 20 and 40 mm of mercury there was rarely a difference of more than 4 mm between the actual pressure and the tonometric reading. One Baillart tonometer was tested and found entirely inaccurate. McLean readings between 20 and 30 mm were 3 mm higher than the Schiøtz and between 30 and 40 mm were 4 mm higher than the Schiøtz.

Four Schiøtz instruments were taken at random and compared. For pressures between 20 and 30 mm, there was no more than 3 mm difference in the readings. At higher pressures, greater inaccuracies developed, but the inaccuracy was constant for the particular instrument and when known could be allowed for in the readings.

The authors stated that for accurate readings the plunger of the tonometer must be absolutely clean, the foot plate must rest smoothly on the cornea approximately on the center and the tilt of the instrument must not be more than 15 degrees. Weights for the Schiøtz instrument should be selected so that the pointer reads between 3 and 7.

19 Adler, F. H., Berner, G. E., and Meyer, G. P. A Comparison of Tonometers for Their Clinical Accuracy. Summary (A. G. Fewell), *Am. J. Ophth.* 19:49, 1936.

Friedenwald⁴ in 1937, in a brilliant "Contribution to the Theory and Practice of Tonometry," presented an analysis of his studies of the structural rigidity of the eyeball and the influence of this variable in tonometry. This comprehensive and for the most part mathematical treatise was unquestionably the most important advance in many years in the field in which there has been a "relative paucity of original studies and of new developments"²⁰. As a result of this study, as pointed out by Harrington and Parsons, three of the major variables in a tonometric reading have so far as theoretically possible been mathematically reduced to constants. The potential accuracy of impression tonometry has thus been greatly increased.

Friedenwald reemphasized that tonometric measurements are not direct measurements of intraocular pressure but are measurements of the degree of indentation of the cornea by the tonometric plunger with a given load. As was noted by the earliest writers on tonometry, this measurement is not dependent on the intraocular pressure alone but is influenced, as has already been stated, by other factors, of which the distensibility of the eyeball as a whole is the most important.

Friedenwald's purpose was to obtain if possible some measure of this resistance to deformation and some indication of the appropriate corrections in pressure readings which variations in such resistance should dictate. "If," he stated, "we compare two eyes which actually have the same intraocular pressure but which differ markedly in the rigidity or distensibility of their coats, we will erroneously conclude from the tonometric reading that the pressure in the more rigid eye is higher than in the more distensible eye." This study represented an attempt to disentangle these two factors in the tonometric reading.²¹

For it Friedenwald used the Schiøtz tonometer with its original concave plunger end of the same radius of curvature as the tonometer foot plate, he omitted all consideration of the rounded plunger of the Schiøtz x-tonometer and of the plunger of the McLean¹⁶ instrument. He stated, first, that more extensive experimental and clinical data exist for this type of plunger and, second, that the theoretic development of the relations which he sought are simpler when this form is considered.

When the Schiøtz tonometer is placed on the eye, a twofold effect is produced. Since the foot plate has a radius of curvature of 15 mm, while the radius of curvature of the cornea in normal eyes varies from 7 to 8 mm, the cornea must be flattened over the area of contact with the tonometer. In addition, the plunger indents the cornea, and it is the depth of the indentation from the level of the foot plate that is read on the tonometer scale.

"When the plunger indents the cornea," the author continued, "fluid is displaced from beneath it, and the intraocular pressure is raised. Part of the displaced fluid may be accounted for by an expulsion of blood from the intraocular vascular bed and an actual absorption of fluid out of the ocular cavity, while the remainder can be accommodated only by a distortion of the eyeball as a whole, no doubt mainly by an expansion in the equatorial zone of the eye."

Friedenwald stated that experimental work has shown that a measure of the compressibility of the intraocular vascular bed is included in the elasticity measurement, while the expulsion of intraocular fluid from the interior of the eye, as a result of the massaging effect of the tonometer, does not introduce important errors if the tonometric measurements are done rapidly.

²⁰ Terry, T. L., in discussion on Harrington and Parson,³ p. 228.

²¹ Friedenwald, J. S. Contribution to the Theory and Practice of Tonometry. Condensed Summary (A. G. Fewell), *Am J Ophth* 21: 193, 1938.

Perhaps it would be best to quote Friedenwald directly in regard to the general plan of his study

We have first attempted a theoretical analysis of the factors involved in a tonometric reading and have grouped together for consideration those factors other than pressure which may be thought of as contributing to the resistance that the eyeball exhibits to indentation by the tonometer. Previous studies on the elasticity of the eye are then considered, and from the experimental data recorded by other observers a mathematical law is derived of the relation between volume and pressure changes in the eye, together with a mathematical formulation of what may be regarded as the coefficient of rigidity of an eyeball independent of pressure. This law is then applied to tonometric readings on the assumption that the application of the tonometer with successively different weights to an eye produces in the eye successively different pressure and volume changes. In order to accomplish this, it is necessary to know the volume of the corneal indentation produced by the tonometer plunger, and the intraocular pressure at the time when the tonometer is resting on the eye. The latter can be computed directly from the data given by Schiøtz in the original measurements which he made in order to calibrate his tonometer. The former may be calculated to a fair approximation. It follows that with the aid of these calculations the coefficient of rigidity of an eye can be computed from a pair of tonometric measurements made with two different weights. By allowing for the distortion of the cornea produced by the tonometer foot plate, the intraocular pressure that existed before the application of the tonometer on the eye may be estimated. A chart or nomogram has been constructed with the aid of which these otherwise laborious calculations can be performed graphically.

The second stage of the investigation has consisted in applying these methods for the measurement of the rigidity and pressure first to normal and then to abnormal eyes. A statistical analysis of the results on normal eyes has enabled us to evaluate the effect of age, sex, axial refraction, and corneal curvature on intraocular pressure and ocular rigidity as determined by this method. The average normal ocular rigidity is found to be somewhat lower than that implied in the data used by Schiøtz to calibrate his tonometer, and the average normal intraocular pressure is found to be correspondingly higher than that assumed by Schiøtz. Using these data, a correction for the Schiøtz chart or nomogram is obtained. Finally, the results of measurements of ocular rigidity and pressure in certain diseases are presented, and also an analysis of the effect of certain drugs on the rigidity and pressure of the eye.

Friedenwald based his experimental work on the data reported by Schultze, Koster, Schiøtz, Ridley and Clark on the distensibility of the eyeball and on the experimental data which Schiøtz used in computing his 1924 scale of pressures. In regard to the latter, Friedenwald stated, "The extraordinary perspicacity with which Schiøtz analyzed his own results has been a recurring source of help to us in our study." Harrington and Parsons, also commenting on the experimental data supplied by Schiøtz, stated that the final measurements and calculations from which Schiøtz computed his 1924 scale of pressures are models of scientific care.

By using the data on which Schiøtz based his tonometric chart, Friedenwald computed the pressure which exists within the eye at each tonometric scale reading for each weight of the tonometer plunger and also the volume of the indentation corresponding to each tonometric scale reading. With the aid of these calculations and an empiric formula for the relation between pressure and volume changes in a given eye based on the experimental work on ocular distensibility, a nomogram was developed from which the coefficient of an eye may be computed from two tonometric readings with two different weights. (Measurements were made routinely on normal eyes with the 5.5 and 10 Gm weights and in the cases of elevated tension with the 7.5 and 15 Gm weights. In a few instances all four weights were used.) Finally, by allowing for the distortion of the cornea due to the tonometer foot plate irrespective of the indentation produced by the plunger, a method was developed for calculating the true intraocular pressure free from errors due to the rigidity of the ocular coats.

Having determined the average rigidity coefficient of normal emmetropic eyes, Friedenwald was in a position to recompute the Schiøtz scale so that tension read-

ings made with its aid would be accurate, at least when the ocular rigidity was normal. This chart is based on the assumption that the tonometer used is, in fact, an accurate mechanical replica of the standard Schiøtz tonometer.

The average normal pressure determined with such an instrument by means of this chart will be found to be 25 mm of mercury. Readings above 35 mm are to be attributed to either abnormally high pressure or abnormally high rigidity. If measurements on an eye are made with two different weights and the same pressure is indicated on the chart with each weight, the eye may be considered as having normal rigidity and the pressure reading as accurate. If with the heavier of the two weights the apparent pressure reading is higher, the eye is abnormally rigid, and the actual intraocular pressure is lower than either of the two readings. If with the heavier weight the apparent pressure reading is lower, then the eye is abnormally distensible, and the actual intraocular pressure is higher than either of the two readings would indicate.

Friedenwald found that the rigidity of the eye is increased in old age and in extreme myopia. This is likewise the case in intraocular inflammatory disease and not infrequently gives rise to an erroneous diagnosis of secondary glaucoma. In primary glaucoma, the ocular rigidity tends to be increased by long-continued high pressure. The effect of certain drugs on the ocular rigidity has been studied, and it was found that those drugs which act as vasodilators tend to diminish ocular rigidity and those which act as vasoconstrictors tend to increase ocular rigidity. The cause of the relative increase in the rigidity of the eyeball in extreme myopia has not been ascertained. The possibility that the sclera has been stretched beyond its elastic limit is suggested.

Harrington and Parsons³ supplemented the work of Friedenwald and in 1941 presented a paper on a method of increasing the accuracy of tonometry. This valuable study will undoubtedly go far toward achieving the long sought goal of tonometric standardization.

Following in the footsteps of Schiøtz and Friedenwald, who, they declared, have done most to point out the need for tonometric standardization, Harrington and Parsons stated:

We have made a searching analysis of Friedenwald's work and are entirely in agreement with his theory and his conclusions, all of which we have accepted in toto as logical and in definite order. We feel, however, that the work exhibits several drawbacks which have robbed it of some of the appreciation that should have been its due, and while we are unable to add to the fundamental concepts involved it seems highly desirable to make better use of these concepts by presenting them in somewhat less abstruse form and in such a way as to make them easily applicable to clinical tonometry.

We make no attempt within the limits of this paper to review the vast subject of tonometry. We are content with the more modest aim of using the salient points presented by various authors to evolve a clinically workable method of tonometry and one which we feel is more accurate in its interpretation of tonometric readings. Schiøtz' experimental work is readily available, but it remained for Friedenwald to coordinate it in such a manner as to eliminate the important variable of the resistance to pressure which is exerted by the rigidity of the ocular envelope and thus make it possible to determine to a reasonable degree of approximation the actual resistance to tonometric pressure exerted by the intraocular pressure alone. The assumption of an average rigidity of ocular coats thus becomes inadmissible.

Friedenwald's work has served to emphasize the fundamental accuracy of the findings of Schiøtz. If one accepts the validity of the theory that ocular rigidity is a prime factor in the determination of actual intraocular pressure, one must automatically accept the principle of the tonometer with multiple weights and a concave plunger. Schiøtz anticipated us in this when he convinced himself that his own X tonometer added nothing of value sufficient to warrant its adoption.

Clinical application of the increased accuracy of interpretation contributed by Friedenwald to the Schiøtz method plus the vast accumulation of clinical data based on the Schiøtz scale,

plus the practically international acceptance of the Schiøtz nomogram, provides a widely used, clinically accurate method of impression tonometry as capable of rigid standardization and universal adoption as the Snellen visual acuity test. It remains but to devise an instrument by which this method may be fully utilized.

As has already been noted, Schiøtz was much distressed by the tendency to record tonometric readings in terms of millimeters of mercury. Harrington and Parsons said

In spite of his exhortations the clinical use of direct pressure recording has persisted and, it cannot be denied, has much to be said in its favor. This attempt at a more direct approach to the analysis of intraocular pressure has, through wide clinical use and common consent, succeeded gradually in almost replacing the original Schiøtz method. It is largely responsible for the search for satisfactory direct reading instruments, such as those designed by McLean and Baillart.

It is indirectly responsible for the confusion and lack of standardization in tonometry today.

The authors stated that the Schiøtz tonometer in its present form is not a standardized instrument in any sense of the word. They carefully checked the weights and measurements of a large number of such tonometers, some manufactured in Europe and some in the United States. They found no instrument that adhered to Schiøtz' original specifications and no two instruments that were alike in more than the diameter of the plunger.

Harrington and Parsons undertook to analyze, simplify and recalculate what they termed the fundamentally sound principles presented by Friedenwald, in order to make them practical for clinical application. As a substitute for the graph method of calculating ocular pressure and rigidity, as proposed by Friedenwald, they presented a simple numerical chart from which the true intraocular pressure may be read when two tonometric readings are taken, each with a separate weight. In addition, they presented a new tonometer, designed to minimize reading errors, adhering rigidly to fundamental specifications and capable of use as a multiple weight instrument according to the directions of Schiøtz or, with the new numerical chart, according to the method of Friedenwald. It is also, within the natural limits of any multiple weight tonometer, a direct reading instrument.

Friedenwald²² agreed that the numerical chart has much to be said for it in respect to convenience, but he cautioned that such a table of numbers may readily give a false sense of exactitude. One must keep constantly in mind, he counseled, the range of probable error in the measurement. As for the new instrument, he stated

I have had the opportunity to see a photograph of Dr. Harrington's tonometer and have been much impressed with its appearance. I have not had an opportunity to study the instrument itself and should prefer to reserve judgment about it. There can be no doubt, however, that the authors are decidedly on the right track. The slovenliness in construction of Schiøtz-type tonometers sold at a substantial price in this country is really shocking. I once weighed half a dozen instruments all produced by the same manufacturer and found variations of 2 Gm. or more in the weight of the parts which rest on the tonometer foot plate and of over 1 Gm. in the weight of the plunger and the lever arm. It would seem that the manufacturer is unaware that the mark 55 which he has engraved on the instrument means 55 Gm.

I believe that the authors will agree with me in the assertion that standardization of the tonometer should include rigorous definitions of the permissible variations from the standard.

Further desiderata are as follows:

The scale should be close to the eye, as in the McLean tonometer. The center of gravity of the whole instrument should be low. The plunger should have the concave end and variable weight of the Schiøtz model rather than the convex end of the Schiøtz X model and of the

22 Friedenwald, I. S., in discussion on Harrington and Parsons,³ p. 224.

McLean¹⁶ instrument In addition, the instrument should be rugged and easily disassembled for cleansing, with its more delicate moving parts enclosed and protected It should be reasonably inexpensive

It is evident that many of these requirements are fulfilled by the instrument shown

T L Terry,²⁰ in discussing the paper of Harrington and Parsons stated that it would not be difficult to raise objections and criticisms, chiefly because impression tonometry, or for that matter any form of tonometry, is through necessity not scientifically accurate, especially if the tension reading is taken directly in terms of intraocular pressure Perhaps the foot plate is not curved in the best form, perhaps the plunger should be larger or smaller for best results

He stated that the perfect solution of the problem of determining the actual intraocular pressure as a clinical test lies in the development of the best substitute for manometric determination, a solution which would require in combination a physiologist, a physicist and an expert mechanic skilled in the minute accuracies of the watch maker He said

True, the Schiøtz type of instrument is the most popular and does seem to be the most satisfactory, yet if as much time and effort were spent on study and use of the other general types, as represented by the Souter, the aplanation and the recoil tonometer, perhaps they would be found as good or better Harrington and Parsons are to be complimented for designing a new impression tonometer and for explaining its apparent superiority with broad consideration of the many obstacles incident to tonometry Such work as theirs requires the utmost patience, time and skill The instrument will be its own best critic once it has been tested thoroughly by critical clinicians This instrument is well worthy of trial before any objections are to be considered It is my hope that the findings of Harrington and Parsons will be substantiated and that the ophthalmologist will find that the new tonometer is all that it appears to be—superior not only to other impression tonometers but to other types of tonometers

Mention has been made of the Souter²³ tonometer This is a well balanced spring instrument about the size and weight of a fountain pen, simple in construction and in method of application It gives direct readings which are taken with the patient upright Lloyd² has stated that the accuracy of this instrument is not to be compared with that of the Schiøtz and the McLean, but that if readings with the patient upright were desired his choice of instrument would be the Souter rather than the Baillart Harrington declared that the spring element would tend to introduce inevitable inaccuracies in the readings of a tonometer of this type Verhoeff,²⁴ on the other hand, has relied on the Souter tonometer for over twenty years He has stated that in the use of this instrument all variables pertaining to the eye other than the actual intraocular pressure become relatively unimportant, that this tonometer is more precise than the Schiøtz and that it gives a more accurate indication of the actual intraocular pressure in the living eye than is usually obtained even by laboratory methods Verhoeff declared that, in addition to its greater accuracy, the Souter tonometer has two important advantages over the Schiøtz instrument It is less dangerous to use from the standpoint of possible corneal abrasion and it is less objectionable to the patient The one disadvantage, he stated, rests in the difficulty of determining the amount of indentation of the cornea at which the instrument is to be read, but once one has acquired this ability by practice there is less difficulty in making readings with this instrument than with the Schiøtz

23 Souter, W N Simple Tonometer for Clinical Use, *Ophth Rec* 25 80, 1916

24 Verhoeff, F H The Souter Tonometer, *Am J Ophth* 20 720, 1937

When Ferree and Rand,⁵ in 1931, introduced and described an apparatus which they had constructed as a checking standard for tonometers, they called attention to a definite shortcoming in connection with the clinical test of tonometry

In a survey of the literature it is amazing to see how much work and ingenuity have been expended on the devising of tonometers of different kinds and how little attention has been given to means for checking them for constancy and uniformity of performance. There seems to be no type of test or measurement in the practice of ophthalmology more acutely in need of standardization than tonometry

In 1942 Reese,²⁶ with the evidence of his own experiences and those of Friedenwald and Harrington and Parsons at hand, gave reemphasis to this situation saying

There is a tendency among ophthalmologists to accept the readings of a tonometer without questioning the instrument's accuracy, but tonometers should not be relied upon implicitly unless they have been checked and their accuracy or margin of error established

The Schiøtz tonometer is employed more than any other, and its mechanical accuracy is of the very first importance, since the nomogram, or chart by means of which the readings are converted into millimeters of mercury, is based on an instrument designed by Schiøtz and having definite and precise specifications. When we buy a Schiøtz tonometer we are paying the price of, and expect to secure, an instrument of precision. Unfortunately, such is usually not the case

Reese stated that checking stations for Schiøtz tonometers were established in Tübingen by Arnold, in Oslo by Schiøtz and in Berlin by Comberg in 1923, 1925 and 1928, respectively, but that we did not have such a checking station in this country until 1935. At that time, at the suggestion of Dr. Mark J. Schoenberg, a station was established at the Hermann Knapp Memorial Eye Hospital, New York, by Dr. Adolph Posner. During the several years this station functioned, Dr. Posner checked about two hundred tonometers and found about one third of them to be incorrect, the majority of these were of American make. Reese stated the belief that checking stations for tonometers should be conducted in this country and that ophthalmologists should feel morally compelled to have their instruments certified at such stations.²⁷

There is no gainsaying the fact that within recent years the efforts of Friedenwald and of Harrington and Parsons have resulted in valuable contributions toward the long sought goal of standardization. As further evidence of the recognition of this need, a committee known as the Committee on Standardization of Tonometers, consisting of Drs. Adler, Friedenwald, Posner, Gifford, Kronfeld, Gradle and Harrington, was recently appointed²⁸ on recommendation of the Council of the American Academy of Ophthalmology and Otolaryngology

99 Lafayette Avenue

25 Ferree, C. E., and Rand, G. A Checking Standard for Tonometers, *Arch Ophth* 6: 689 (Nov.) 1931

26 Reese, A. B. Standardizing and Checking Tonometers, *Am J Ophth* 25: 478, 1942

27 A station for checking the accuracy of original Schiøtz tonometers is maintained at the headquarters of the National Society for the Prevention of Blindness, 1790 Broadway, New York. In reply to an inquiry, the society reported that at the present time this checking station is the only one in the United States

28 *Tr Am Acad Ophth* 47: 138, 1942

Obituaries

JOHN MILTON GRISCOM, M D 1881-1943

J Milton Griscom was born in Salem, N J, Feb 23, 1881 and died June 5, 1943, at the Pennsylvania Hospital, in Philadelphia. While he had endured with fortitude much suffering from a sinus and allergic condition for seven years, there had been no evidence or suggestion of cardiovascular disease. His first



JOHN MILTON GRISCOM, M D
1881-1943

attack came suddenly, on June 3. He was taken home and two days later was removed to the Pennsylvania Hospital, where he died that evening of coronary thrombosis. He was the son of Walter Davis Griscom and Mary McIlvaine Bessett, members of the Society of Friends.

His early education was acquired at Friends' School and the Swarthmore Preparatory School. He entered Swarthmore College and graduated with the degree of Bachelor of Science in 1902. His years at Swarthmore were always

pleasant memories. His jovial manner and musical talent as a member of the college glee club attracted many friends, who were loyal throughout the years. It was here he met Mary Lippincott, whom he married in October 1915.

Within a few weeks after he received his degree at Swarthmore, his father was appointed superintendent at Wills Hospital. This fortunate coincidence was the deciding factor in young Griscom's medical career. He was admitted to the medical school of the University of Pennsylvania and graduated with the degree of Doctor of Medicine in 1906. He then served one year as intern at the Germantown Hospital, in Philadelphia.

His career at Wills Hospital began as intern in 1908 and continued for a span of thirty-five years. The staff at Wills during this period included such eminent men as Oliver, Posey, Zentmayer, Ziegler and Sweet, all members of the American Ophthalmological Society. From these men he gained not only a thorough knowledge of ophthalmic practice and surgery, but a strict rule of ethics, which he practiced to the end. He was assistant surgeon in 1910, attending surgeon in 1926 and executive surgeon for the past several years.

In 1914 he was elected to the American Ophthalmological Society. His interest and devotion to this society was attested by his work. From 1929 to 1933 he served as editor of the *Transactions*, from 1933 to 1937, as secretary-treasurer, and from 1938 to 1943 as member of council.

When the Graduate School of Medicine of the University of Pennsylvania was organized, Dr. Griscom was made associate professor, and shortly after professor, of ophthalmology. He served as consultant to the Jeanes Hospital, Philadelphia, and to the Burlington County Hospital, at Mt. Holly, N. J. He was a member of the American Medical Association, the Philadelphia County Medical Society, the Medical Society of the State of Pennsylvania and the American Academy of Ophthalmology and Otolaryngology.

He was elected fellow of the College of Physicians of Philadelphia in 1912. He served as clerk of the section on ophthalmology of this society and later as chairman. During his early years he presented a number of interesting cases and papers before this society. Dr. Griscom was not a frequent writer, but he contributed freely of his time in lectures before the ophthalmic section of the Philadelphia County Medical Society. He was a member of Phi Kappa Psi fraternity and the Union League.

He is survived by his wife, a daughter, Mary Lippincott Jr., and a sister, Mrs. J. Passmore Elkinton. Since his marriage he had lived in Moorestown, N. J., where he took an active interest in the Friends' School. He was devoted to his family and enjoyed the comfort of his delightful home above all. His vacation was usually spent at Buck Hill in the Pocono Mountains, where for many years he enjoyed and played an excellent game of golf.

It was my privilege to know Dr. Griscom intimately since our initial meeting at a meeting of the American Ophthalmological Society at New London, Conn., in 1915. He was a gentleman, quiet in manner, unassuming and conscientious, and gave the best that was in him to the service of his patients.

CHARLES R. HERD

LESLIE J PATON, M.B., F.R.C.S
1872-1943

Leslie Paton died in London on May 15, after a long illness. Born in Edinburgh, Scotland, in 1872, the second son of James Paton, F.L.S., curator of picture galleries and museums, he received his early education in the Glasgow high school and the University of Glasgow and at Caius College, Cambridge University. He graduated from the medical school of St Mary's Hospital, London, with the degree of Bachelor of Medicine, and received the qualification of Fellow of the Royal College of Surgeons in 1902. Paton began his ophthalmologic studies as assistant to Henry Juler at St Mary's Hospital and succeeded him in the post of ophthalmic surgeon in 1911. He also worked with Marcus Gunn, both at Moorfields and at the National Hospital, Queen Square, and was appointed Gunn's successor as ophthalmologist to the National Hospital in 1907, where he had the privilege of following the teachings of that great neurologist Hughlings Jackson. Paton had the double distinction of being chosen president both of the Neurological Section of the Royal Society of Medicine and of the Ophthalmological Society of the United Kingdom. As suggested by his training, one of his principal interests was in ophthalmic neurology, and his chief, and most important, contributions to ophthalmic literature were on neurologic subjects, such as "The Pathology of Papilloedema," in collaboration with Gordon Holmes, "Optic Atrophy in Tabes," and his Mackenzie Memorial Lecture in 1937, "Demyelinating Diseases accompanied by Optic Neuritis." His administrative capacity had full play in the important work that he performed as treasurer of the International Ophthalmological Council and as managing director of the *British Journal of Ophthalmology*, when he conducted the affairs of that journal to safety in the difficult years after the first world war.

Leslie Paton was tall and handsome, a kindly and strong personality, thorough and earnest in his work, and his death is a great loss to ophthalmology and to his many friends. As Dr Wilfred Hailes¹ stated:

Leslie Paton made few, if any, enemies, though he was highly successful in practice. His brain was brilliant and analytical, but he took his time in making up his mind. Though unknown personally to the present generation of students at St Mary's he will be long remembered by his friends and generations of past students for his teaching, his balanced mind, and his cheery disposition.

ARNOLD KNAPP

I was resident medical officer at the National Hospital from 1907 to 1910 inclusive, nearly four years, during which time Mr Marcus Gunn and Mr Paton were the attending ophthalmologists of the hospital. Mr Paton made rounds once or twice every week and taught the value of careful study and the importance of small things. His interest in our first case of ipsilateral optic nerve atrophy and contralateral papilledema, occurring as a result of a meningioma of the sub-frontal region, was great, and his encouragement led me to further studies on this and other ophthalmic problems occurring in neurologic medicine.

Mr and Mrs Paton were exceedingly kind to me, almost giving me the run of their house in Hailey Street. Both of them remained as Scottish as the "Kyles of Bute" and their kind lives were illuminated always by their cheery hearts and pawlish humor.

¹ Leslie J Paton, Obituary, Brit M J 1 741 (June 12) 1943

I have seen Paton practically every year since my acquaintance with him and had the pleasure of a long letter from him last year, after his daughter and son-in-law had paid us a week's visit in Bar Harbor

By his death the neurology of the eye has lost perhaps its most distinguished exponent, and I have lost one of my closest friends

FOSTER KENNEDY



LESLIE J. PATON, M.B.
1872-1943

In the death of Leslie Paton, his family and friends have suffered an irreparable loss and ophthalmology has lost one of its outstanding members. His keen mind and tenacious memory gave him a fund of information that was most unusual

Every one who visited Queen Square while he was on duty could not but be impressed with the sincerity of his work and the meticulous and broad manner in which he considered his cases. His ability as an organizer is well shown in the part he played in the reorganization of the International Congress of Ophthalmology after World War I.

He was tireless in his efforts, and all who were associated with him appreciated fully his sincerity and fairness in his methods of procedure. His sterling honesty, his calm demeanor and his grasp of every situation that presented itself were greatly admired by all who were associated with him.

It was a great privilege to know Leslie Paton and to become acquainted with his quiet, untroubled nature and his wise counsel. His death leaves a gap which cannot be filled, but all are richer for the inspiration and example of his life.

WALTER R. PARKER

News and Notes

EDITED BY DR W L BENEDICT

SPECIAL NEWS

Leslie Dana Gold Medal Award—Dr Walter B Lancaster, of Boston, has been awarded the Leslie Dana Gold Medal. This medal is awarded annually for outstanding achievements in the prevention of blindness and in the conservation of vision. The selection of Dr Lancaster for this honor was made by the St. Louis Society for the Blind, through which the medal is offered by Mr Leslie Dana, of St. Louis, on recommendation of the Association for Research in Ophthalmology.

The conditions of the Leslie Dana Medal award set forth that it is to be made for "long meritorious service in the conservation of vision in the prevention and cure of diseases dangerous to eyesight, research and instruction in ophthalmology and allied subjects, social service for the control of eye diseases, and special discoveries in the domain of general science or medicine of exceptional importance in conservation of vision."

Notice

If the demand is sufficient, the American Medical Association Press will reprint the series of lectures by Prof Alfred Bielschowsky on Motor Anomalies of the Eyes, which was published in the December 1934 issue of the ARCHIVES page 805 and in the January, April and May issues of 1935, pages 33, 569 and 751.

A form is printed below for the convenience of those who wish to order the reprint. The price will depend on the number of reprints ordered, but it will not exceed \$2.50.

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ADIE'S SYNDROME

To the Editor —Dr Rooks's article "Adie's Syndrome," in the June issue (ARCH OPHTH 29:936, 1943) suggests that all cases of this syndrome "be brought to the attention of the medical profession with as much publicity as possible." I am in complete agreement with this idea, and I assume that if this is the purpose of the report, the cases which are described should be typical of the syndrome, should not be unusual and misleading varieties, should be carefully, completely and fully worked up, and should leave no doubt in the reader's mind as to just what the Adie syndrome is. I am aware that in conclusion the author states

these 2 cases are offered for their clinical and scientific importance, with the hope that further interest in the study of Adie's syndrome may be stimulated, but my limited knowledge of the fundamental nature of this disorder warrants no specific conclusions.

The first case presented was that of a man aged 44. A definite history of head injury was noted eighteen months and inequality of the pupils eight weeks prior to examination.

The left pupil was 5.5 mm in diameter and firmly fixed. Prolonged exposure to bright artificial light or to direct sunlight failed to produce any change whatever in the size and shape of the left pupil, nor did its size and shape change after the patient remained in a completely dark room for thirty minutes. The left pupil remained dilated and absolutely inactive to light and accommodation.

These many statements require elucidation, for the findings are atypical of Adie's syndrome and serve to confuse, rather than to clarify, the clinical picture. It has been pointed out (and by men to whom the author refers, viz., Adie, Saenger, Strasburger and Behr) that the most consistent, the most easily recognized and for diagnostic purposes the essential feature of this syndrome is the behavior during and after convergence. The author states that the myotonic pupil may be "incompletely or entirely indifferent to convergence and to accommodation." Such a response is an exception to the rule, and in Alajouanine and Morax's review of 100 cases this was rarely reported.

Dimmer, Behr and Lowenstein stated (and it is now established) that the second most characteristic feature of the syndrome is dilatation of the Adie pupil when the patient remains in darkness for one hour and that when the patient comes out into the light a sluggish contraction of the pupil occurs after an interval.

Most cases of the Adie syndrome occur in young persons, and most of the patients are highly emotional—case 1 fulfils neither of these requirements.

In the second case outstanding discrepancies are the patient's age, the absence of the characteristic delayed reaction to convergence and the pronounced pupillary irregularity. Again, a question arises as to the bilaterality of the syndrome inasmuch as the left pupil was 3.5 by 2.5 mm and reacted "well both to light and in accommodation." Since the Adie syndrome is one of "mid mydriasis," with no normal reaction to light or to accommodation, this statement is contested, especially since Behr asserted that "a pupil not more than 3 mm in diameter is never an Adie pupil."

Many other tests and features might have been used to clarify the syndrome, such as tests of accommodation, fatigue of accommodation, superimposition of convergence on accommodation and its effect on size of the pupils. The reaction to various drugs, such as mechoyl, strychnine, cocaine and physostigmine, as pointed out by Cogan, Adler, Kyriehies and Lowenstein, might add certainty to the diagnosis. A history of vasomotor changes and emotional disturbance and a study of other ocular reflexes might also be considered.

I believe every case of this syndrome should be reported and completely worked up and if such reports are for the benefit of the "medical profession" then typical rather than atypical forms of the disease should be reviewed.

EMANUEL ROSEN, Captain M C, A U S

Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

Anatomy and Embryology

FUNCTIONAL REPRESENTATION IN OCULOMOTOR AND TROCHLEAR NUCLEI M B BLINDER and E A WEINSTEIN, Arch Neurol & Psychiat 49:98 (Jan) 1943

The article deals with localization of function in the cell masses of the oculomotor nucleus. Electric stimulations and lesions were made in the oculomotor and trochlear nuclei of monkeys. The experiments indicate that individual ocular muscles are functionally represented within the ipsilateral oculomotor nucleus, while the superior oblique muscle is governed by the contralateral trochlear nucleus. The dorsoventral and rostrocaudal arrangement of functional representation of the ocular muscles is as follows: (1) sphincter pupillae, (2) inferior rectus, (3) ciliary (?), (4) inferior oblique (?), (5) internal rectus, (6) superior rectus, (7) levator palpebrarum, (8) superior oblique (contralateral) R IRVINE

Conjunctiva

MEMBRANOUS INFLAMMATION OF OROPHARYNX, NOSE AND CONJUNCTIVA DUE TO SULPHATHIAZOLE ADMINISTRATION I M SCHNEE, Brit M J 1 506 (April 24) 1943

The following case is reported as evidence of an unusual type of toxic reaction from therapy with a sulfonamide compound. The reaction consisted in inflammation involving the conjunctiva, nose, pharynx, mouth and larynx, with the development of a membrane. There was rapid recovery on discontinuance of the chemotherapy.

The patient, a soldier 28 years of age, had been treated with sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) for an infection of the upper respiratory tract. After he had received about 18 Gm the symptoms seemed to be relieved and treatment was stopped. On the fifth day of chemotherapy the eyes became inflamed and a discharge was present, then the mouth became very sore and the lips cracked. The fever recurred, and the patient was sent to the hospital. The lids were swollen with a smooth, thick, well formed gray membrane which left no bleeding surface when peeled off but reformed within a few hours. The cornea was not involved. A similar condition was found in the mouth and throat. Smears and cultures were negative except for staphylococci. On the patient's relapse, sulfathiazole treatment was renewed. When the condition of the eyes and throat became worse, at the suggestion of Lieut Col Derrick T Vail use of the drug was discontinued. The patient rapidly became well.

ARNOLD KNAPP

Congenital Anomalies

ANOMALOUS PROCESSES OF CILIARY TYPE ON POSTERIOR SURFACE OF IRIS S GARTNER, Am J Ophth 25 854 (July) 1942

Gartner gives the following summary:

"Twenty-six cases are reported of anomalous processes on the posterior surface of the iris. They closely resemble the ciliary processes, from which they are separated by normal iris tissue. The anomalous processes are fetal remains of

tissue which usually disappears by the time of birth. Their presence can assume practical importance in complicating an iridectomy, in as much as they may cause increased hemorrhage and postoperative reaction"

W S REESE

DISPLACEMENT OF CILIARY PROCESSES TO POSTERIOR SURFACE OF IRIS S
GARTNER, *Am J Ophth* 25:858 (July) 1942

Gartner gives the following summary

"Partial displacement of ciliary processes to the posterior surface of the iris is a common variation from the normal. This is explained by the embryology of the ciliary processes. Its importance in iridectomy is discussed"

W S REESE

Cornea and Sclera

CASE OF BILATERAL INTERSTITIAL KERATITIS LEADING TO BLINDNESS J D J
FREEMAN, *Brit J Ophth* 27:104 (March) 1943

The patient was a stoker aged 19. The morning after a "blitz" during which, without incurring injury, he noted a "very bright flash," the left eye became inflamed. Examination showed beginning interstitial keratitis. In about six weeks the eye was shut and blind. There was panophthalmitis, and the cornea had evidently perforated. The eye was excised. About eleven weeks from the time the left eye became inflamed, interstitial keratitis developed in the right eye. The outcome was an opaque cornea, a soft eye and vision equal to light perception. The Wassermann reaction of the blood was strongly positive. The treatment was directed to the syphilitic infection, and later a course of tuberculin was given. The author describes the case as one of very severe congenital syphilitic infection of the eyes starting as interstitial keratitis and going on to bilateral gummatous infiltration of the uveal tract and loss of both eyes

W ZENTMAYER

CONTACT LENS IN CASES OF NEUROPARALYTIC KERATITIS M KLEIN, *Brit J Ophth* 27:221 (May) 1943

After an operation for an acoustic tumor on the right side the patient had complete palsy of the right facial nerve and trigeminal anesthesia. Neuroparalytic keratitis developed, for which a tarsorrhaphy was done. After a year, though the lids were still sutured, the condition of the eye seemed hopeless. In August 1942 the patient was fitted with a contact lens. Rapid improvement followed, and within two or three weeks the eye became white and the cornea cleared considerably except at the central area, where a dense scar remained. In November 1942 the patient broke the contact lens, within a few hours the eye became inflamed and the following day the infiltration was extensive. A new glass was supplied, and within a week the eye quieted down.

In a second case, in which neuroparalytic keratitis developed, with involvement of the cornea, after an alcoholic injection for trigeminal neuralgia on the right side, a contact lens gave an equally good result.

W ZENTMAYER

General Pathology

PATHOLOGY OF CHOLESTERIN AND FAT DEPOSITION IN MUSTARD GAS INJURIES OF THE CORNEA I MANN and B D PULLINGER, *Brit J Ophth* 26:503 (Nov) 1942

In a previous paper Mann and Pullinger showed that, of experimentally produced mustard gas lesions of the eyeball, central corneal lesions healed without vascularization of the cornea and did not lead to deposition of cholesterol or fat in the scars. It is therefore considered that the essential factor in this

degeneration is previous vascularization of the cornea. In some cases the vascularization was superficial, this type was never followed by deposition of fat or cholesterol. In other cases the vessels penetrated the substantia propria, with separation of the lamellas by edema fluid ahead of the invading vessels. These deeper vessels showed extremely bizarre shapes and irregular caliber and extended in the form of tips or pointed ends, in which no movement of blood could be seen. The pattern varied from day to day, always extending farther into the cornea and always accompanied by edema. The arrangement of bulbous ends and right-angled branches suggested so-called Bowman canals. As the vessels retrogressed, in a relatively small number of cases a deposit of fat and cholesterol was formed beyond their disappearing tips. It was noticed that the series of eyes which received treatment showed a much higher percentage of degenerative scars than did those in which the lesion was allowed to run its usual self-limited course. The lipoids occur in two forms, as exceedingly fine droplets, like an emulsion, bathing the fibrils of the substantia propria and as larger intracellular globules and crystals having the characteristics of esters of cholesterol.

W ZENTMAYER

Glaucoma

OPERATION FOR CONGENITAL GLAUCOMA O BARKAN, *Am J Ophth* 25 552 (May) 1942

Barkan presents the following summary and conclusions

"In this paper the results of operations on 17 eyes with congenital glaucoma are reported. Pressure was normalized in 16 of the 17 eyes, visual function was maintained in 14. Of the three blind eyes brought to operation, vision was lost in two before surgery was instituted. In only one case did operation fail to normalize the pressure in time to save vision. Sight was preserved in the fellow eyes of these three infants so that they were saved from blindness. The average age at time of operation was three months. From one to five years have elapsed since the operations were performed. On the basis of the successful results and of pre- and post-operative gonioscopy, certain conclusions are arrived at in regard to the underlying pathology and to the mode of action of the operation. It appears that the majority, if not all, binocular cases of congenital glaucoma are due to a developmental obstruction in the excretory angle which, when removed, permits outflow of aqueous into the canal of Schlemm. The canal is found to be present and ready to function in the large majority of cases in which the diagnosis is made at a sufficiently early age, before prolonged distention of the eyeball has obliterated the canal. Early diagnosis and early operation are therefore urgently indicated. The operation gives a high promise of permanent success with a remarkable degree of safety and without disfigurement."

W S REESE

THE PRACTICAL APPLICATIONS OF GONIOSCOPY TO GLAUCOMA SURGERY H S SUGAR, *Am J Ophth* 25 663 (June) 1942

Sugar discusses the practical aspects of gonioscopy in operations for glaucoma, his classification of glaucoma and the clinical picture of acute glaucoma. He briefly reviews the different operations for glaucoma and their indications and efficacy, especially from gonioscopic observations.

W S REESE

GLAUCOMA T H BUTLER, *Brit J Ophth* 27 116 (March) 1943

This is a lecture on glaucoma given during the course for the diploma of ophthalmology at the University of Oxford. It is of sufficient interest to be noted, as many of the views expressed are heterodox but debatable.

W ZENTMAYER

Injuries

REMOVAL OF SMALL MAGNETIC FOREIGN BODIES FROM THE EYE EIGHTEEN MONTHS AFTER THE DATE OF INJURY H NEAME, *Brit J Ophth* 27:226 (May) 1943

The patient was admitted to the hospital because powdered chalk had entered his eye. There was a history of injury to the eye eighteen months before while he was knocking off the head of a screw with a hammer and chisel. There were a corneal scar to the nasal side and a dark rust-colored nodule on the iris behind the scar. The foreign body was freed from the iris and then removed through a keratome section.

The case is reported as an indication that minute magnetic foreign bodies may be retained for a considerable period without setting up appreciable siderosis. The article is illustrated.

W ZENTMAYER

A CASE OF MULTIPLE INTRA-OCULAR FOREIGN BODIES R A D CRAWFORD, *Brit J Ophth* 27:227 (May) 1943

The patient was stamping out steel airplane parts on a hand press when he felt a sting in the right eye. There was a small perforation wound above the center of the cornea, with a track of a foreign body through the lens. In the vitreous there were a fine glistening foreign body about 3 mm long lying antero-posteriorly with one end in the center of the disk, a smaller foreign body at 6 o'clock at the bottom of the vitreous and two minute foreign bodies in the vitreous near the macula. The largest foreign body was found weakly magnetic when the Haab magnet was used under direct ophthalmoscopic observation. The magnet was used once or twice a day for two weeks, at the end of which the body came clear of the disk. After a rest of ten days, the magnet was applied on two successive days, the foreign body came into the anterior chamber but returned through the pupil when the current was turned off. It was removed through a keratome section by hand and giant magnets.

It is suggested that less damage was inflicted than would have resulted from employment of the posterior route.

W ZENTMAYER

Orbit, Eyeball and Accessory Sinuses

SURGICAL TREATMENT OF VASCULAR DISEASES ALTERING THE FUNCTION OF THE EYES A W ADSON, *Am J Ophth* 25 824 (July) 1942

This article deals mainly with pulsating exophthalmos, but aneurysms of the chiasmal region and angiomatous tumors are briefly discussed, particularly with regard to their surgical management.

W S REESE

DIABETES INSIPIDUS AND OTHER UNUSUAL COMPLICATIONS OF ACUTE PURULENT SINUSITIS CLINICOPATHOLOGIC STUDY OF A CASE J C YASKIN, F H LEWEY and G SCHWARZ, *Arch Neurol & Psychiat* 48:119 (July) 1942

The authors report the case of a 21 year old man who showed osteitis of the right lesser wing of the sphenoid bone as a complication of purulent sinusitis. The inflammation spread across the sella turcica and gave rise to changes in the optic nerves. After operation on the sphenoid sinus there developed successively subarachnoid hemorrhage, basilar meningitis and involvement of the floor of the third ventricle, with consequent diabetes insipidus and changes in the cerebrum, which eventually led to generalized convulsions, high fever and death.

Optic neuritis is not a rare complication of disease of the sphenoid and ethmoid sinuses, although there are observers who believe that retrobulbar neuritis is rarely, if ever, due to disease of the paranasal sinuses. In this case it was a striking feature in that the optic nerve atrophy developed during the period of observation in the hospital, in the course of a few days, undoubtedly as a result of the local inflammatory process around the optic chiasm and optic nerves.

R IRVINE

ORBITAL EMPHYSEMA SIMULATING CELLULITIS C L C O'MALLEY, Brit J Ophth 27: 222 (May) 1943

A case is described of severe proptosis, endangering the eye, which followed a stab wound made by a football player's finger. A slight hemorrhage from the eye and left nostril was followed by closure of the eye. Proptosis began on the third day. The cornea became opaque and sloughed at the exposed area. There was marked chemosis, and the eyeball was stony hard. The symptoms were indistinguishable from those seen in orbital cellulitis. An evacuation operation determined that the proptosis was due to gaseous accumulation in the orbit. The eye, which looked a total loss, made an almost complete recovery.

To the author the most likely explanation is that the finger made a valvelike opening in the orbital plate of the ethmoid bone, which allowed air under pressure to enter the orbit.

W ZENTMAYER

Parasites

REMOVAL OF FILARIA WORM FROM EYE M C T REILLY, Brit M J 1 103 (Jan 23) 1943

A middle-aged officer who had spent considerable time in Nigeria requested that a filaria be taken out of his right eye. There was marked injection of the conjunctiva, and a worm could easily be seen wriggling underneath toward the outer canthus. By the time the patient reached the hospital the worm had disappeared, but in half an hour it appeared again in the fornix of the lower sac. The eye was cocaineized, and after a small incision was made the worm was seized with a forceps. Recovery was uneventful. The worm measured 32 mm. The patient had been in England four years since his service in Nigeria. While there he twice had worms removed from his right eye and once suffered from typical "Calabar swellings" on his wrist. Otherwise his health had been good.

ARNOLD KNAPP

FILARIA WORM IN THE EYE E A CHARTRES, Brit M J 1 269 (Feb 27) 1943

The writer says that forty years ago, when he was in northeast India, worms in the eyes were common in horses. It was necessary to immobilize the horse, cocaineize the eye and wait, while kneeling on the horse's neck, for the worm to appear in the anterior chamber, then a knife was plunged slantwise into the anterior chamber and the worm extracted. The worm frequently measured from 1½ to 2 inches (4 to 5 cm). The eye was always inflamed and the cornea opaque with a milky fluid, but cleared up after a few days. The condition if not discovered will destroy the eye.

In Nigeria, filarias are common, and the writer himself, while there, was a sufferer from a worm in the eye, which sometimes caused him inconvenience. He had frequently seen it wriggling in his eye and under the skin of the temple. The trouble lasted six years.

The worms are also common in antelopes.

ARNOLD KNAPP

Retina and Optic Nerve

MARGINAL HAEMORRHAGE ON THE DISC PARTIAL CROSS TEARING OF THE OPTIC NERVE, CLINICAL AND HISTOLOGICAL FINDINGS A LOEWENSTEIN, Brit J Ophth 27:208 (May) 1943

A man aged 38 was injured by a nail which fell on the right eye from a considerable height. A perforating wound was found in the sclera at 4 o'clock, 2 mm from the limbus. There were hyphemia and marked hypotonia. Visual acuity equaled seeing of fingers at 0.5 meter. On clearing of the media a clear arcuate band was visible at the temporal margin of the disk from 11 to 7 o'clock. The breadth was approximately that of a central vein. Later three fine radially situated hemorrhages were present about the disk. The field of vision showed concentric contraction. Judging by the histologic structure of the normal retina the author concludes that the red crescent was caused by the bleeding within the sheaths of the optic nerve, subdural or subarachnoid, with infiltration of Elschnig's border tissue.

Studying the histologic material of excised eyes at the Tennent Institute, Loewenstein found 3 instances of partial cross rupture of the optic nerve at the insertion of Bruch's membrane among a relatively small number of eyes examined. The tears occurred in three different conditions: trauma, hemorrhagic glaucoma and expulsive hemorrhage. All 3 occurred exactly at the insertion of Bruch's membrane. They were produced by instantaneous, probably arterial, subretinal bleeding.

The article is illustrated

W. ZENTMAYER

Trachoma

TRACHOMA ITS PROPHYLAXIS IN ARGENTINA J. A. SENA, *Semana méd* 49:1520 (Dec 24) 1942

According to Sena, about 15 per cent of the population of the world have trachoma. No country in the world is entirely free from it. It is a disease of poverty, promiscuity, unhygienic living conditions and poor food. The diagnosis is difficult. Numerous diagnostic aids have been suggested, such as the complement deviation test, examination for eosinophilia, the phytotoxin test of Macht, the lysozyme titer in the lacrimal fluid, Abderhalden's reaction and the Weil-Felix reaction, but none of these have fulfilled the hopes placed in them. The diagnosis is chiefly clinical and is based on the presence of follicles in the tarsal portion of the conjunctiva, the presence of pannus, the appearance of cicatrices and palpebral and tarsal alterations such as entropion and trichiasis. The treatment is local as well as general. Measures which aim at improvement in the general health should not be neglected. For the incipient forms of trachoma in children mild eyewashes of zinc or copper sulfate are used. The therapeutic armamentarium against the more severe forms includes copper sulfate, silver nitrate, chaulmoogra oil and mercuric cyanide. Physical methods include cauterization and diathermic coagulation. Mechanical methods, such as massage, brushing and curettage, aim at rapid destruction of the trachomatous follicles. Biologic methods occasionally used are autoserotherapy and vaccine treatment. Cicatricial trachoma requires surgical treatment. Opinions are divided as to the efficacy of the sulfonamide compounds. They are of great value in the complicated forms. The disease is most prevalent and is practically endemic in the northern and subtropical parts of Argentina, where it is favored by climatic, social, sanitary and economic conditions. It is not autochthonous for these regions but was brought in by immigrants, chiefly from the Mediterranean countries. Trachoma of children is best combated in the schools. This has been done in recent years with the aid of visiting nurses. Ophthalmologic dispensaries should provide free treatment for adults. Since 1936 the national department of health has provided antitrachoma

drugs for the dispensaries and schools. Mobile medical ambulances would be helpful in bringing treatment to patients in the rural regions. Popular publications, illustrations and moving pictures are valuable in disseminating information regarding the prophylaxis of the disease. J A M A (W ZENTMAYER)

Tumors

INTRACRANIAL DERMOID AND EPIDERMOID TUMORS J MARTIN and L DAVIS,
Arch Neurol & Psychiat 49 56 (Jan) 1943

The definition of epidermoid and dermoid tumors is interesting because of their frequent occurrence about the eye. This article deals with intracranial dermoids and is summarized as follows:

"1 An epidermoid tumor is a benign neoplasm, arising from an embryonic inclusion, or nest of cells. The tumor consists of epidermal cells in various stages of disintegration, together with variable proportions of crystalline cholesterol. This tumor, containing cellular components only from the epidermis, should not be confused with cholesteatoma, which is a product of chronic inflammation.

"2 A dermoid tumor is a benign neoplasm, arising from an embryonic inclusion or nest of cells, the contents of which may represent part or all of the derivatives of the ectoderm.

"3 A teratoid tumor contains representatives from the ectoderm and either one of the other two germinal layers. This tumor bridges the gap between the true dermoid and the true teratoma, which contains components of all three germinal layers.

"In most large series of verified tumors epidermoids are four times as common as dermoids, but in our own group of over 700 verified intracranial tumors this proportion is reversed.

"Epidermoid and dermoid tumors may become manifest at any age, and they do not show any particular relationship to sex, trauma or other incidents in the medical history.

"The dermoid occurs at many different intracranial sites, but is frequently attached to the dura mater, is commonly seen in the midline and most often lies below the tentorium cerebelli. The epidermoid is practically always located in the cerebellopontile angle.

"Frequently roentgenograms reveal local erosion of bone in the skull, with an area of sclerotic bone immediately surrounding the eroded area, and within the eroded space flecks of calcium may be visible. Such lesions should not be regarded as infallible evidence of the presence of an intracranial epidermoid or dermoid tumor, since other intracranial tumors may produce the same roentgenologic changes.

"These tumors may be operated on successfully. In all 5 of our cases the patient has completely recovered from the operation. Two patients who were not immediately relieved of all their neurologic symptoms were greatly improved immediately after operation and are still improving."

R IRVINE

Society Transactions

EDITED BY DR W L BENEDICT

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

RALPH I LLOYD, M D, *President*

W L BENEDICT, M D, *Secretary*

Forty-Seventh Annual Session, Chicago, Oct 11-14, 1942

Embryologic Basis of Extrapapillary Coloboma and Conus President's Address.
DR RALPH I LLOYD, Brooklyn

Symposium on Chemotherapy

OPHTHALMOLOGY JOHN G BELLOWS, M D, Chicago

OTOLARYNGOLOGY CHARLES T PORTER, M D, Boston

INTERNAL MEDICINE JOHN A KOLMER, M D, Philadelphia (by invitation)

Congenital Ptosis: Factors Which Indicate Necessity for Varied Surgical Procedures DR EDMUND B SPAETH, Philadelphia

Pronounced differences in the following factors are characteristic of congenital ptosis (a) the degree of involvement of the levator muscle, (b) the unilaterality or bilaterality of the condition, (c) the presence and degree of accompanying involvement of the superior rectus muscle, and (d) the more extensive complications, such as the jaw-winking reflex and the retraction syndrome. The age and the conditions associated with age at the time the patient appears for operation are also factors.

The variability of these factors indicates conclusively that no single operative procedure can correct more than one set of conditions. The fact that so many operations have been devised for ptosis is proof of this, and not an indication of general dissatisfaction with all forms of surgical treatment of ptosis, as has repeatedly been stated. The mechanical difficulties connected with elevation of a ptotic lid cannot be solved by any single operation. Success means that the patient must have a good functioning lid, i e, it must lift satisfactorily and close normally, and in downward gaze the margin of the lid must follow the movement of the cornea. The winking reflex must be normal, and the patient must have a good orbitopalpebral fold. These requirements can be met most closely by careful study of each case. The surgical procedure which best meets the most important requirements in the case under consideration is the one to be used.

DISCUSSION

DR BERNARD J LARKIN, Indianapolis. Dr Spaeth's able presentation has covered the subject so well that there is nothing to add. The fine organization of his material makes it easy to follow him to his conclusions. He has properly placed congenital ptosis, and this is sufficient reason for appreciative consideration of his research.

He has stressed the importance of early diagnosis and treatment, for in 37 per cent of the cases in his series factors other than epicanthus and ptosis were presented. He suggests that the use of crutch glasses after atropine refraction will assist the child in overcoming these complications, so that operation may be postponed until he is 4 or 5 years old, that not infrequently paralysis of the superior

rectus muscle is of equal importance in production of complications of ptosis which are more serious than the cosmetic blemish, and, that the anatomic classification decides the surgical procedure. He emphasizes the fact that one operative procedure will not correct all forms of ptosis.

He classifies ptosis into nine forms. On first impression it may seem that several of these types are similar, but after careful analysis one must agree with Dr. Spaeth that sufficient conditions exist for such a differentiation. Moreover, this classification becomes especially significant in analysis and presentation of the cases illustrative of the various types. For example, in cases of type 1, unilateral ptosis without involvement of the superior rectus muscles, of type 5, unilateral ptosis with weakness of both superior rectus muscles, more pronounced, however, on the homolateral eye, and of type 8, ptosis associated with the Duane retraction syndrome, shortening of the levator muscle with partial tarsectomy is the ideal procedure. In cases of type 7 recession of the internal rectus muscle may correct this retraction syndrome as well as the ptosis, however, if this procedure is not sufficient, advancement of the levator muscle without tarsectomy will probably correct the condition. Other surgical procedures were necessary in cases of type 5, in which a recession of the overacting right inferior oblique, recession of the left inferior rectus and advancement of the left superior rectus muscle were done. This illustrates the advisability of early operation on the extraocular muscles, before the ptosis is corrected.

"Utilization of the superior rectus muscles has a narrower field of indicatability and permissibility." Dr. Spaeth seems to be the first to advocate still further narrowing of the utilization of the superior rectus muscles in cases of bilateral ptosis by use of a Shoemaker or Kirby modification of the Mottais operation. In a former paper he set forth his reasons for this opinion. The postoperative care of patients undergoing operation on the superior rectus muscle is also more demanding and exacting than that of patients undergoing operation on the levator muscle.

Utilization of the occipitofrontalis muscle, when indicated, is a good procedure to follow, as the author has shown. For type 2, unilateral ptosis with involvement of the homolateral superior rectus muscle, and for type 4, bilateral ptosis with involvement of the superior rectus muscles, the Tansley-Hunt procedure is chosen while for type 6, ptosis with more or less complete paralysis of the third nerve, and even of the sixth nerve, the Reese procedure is indicated. For type 7, ptosis with the classic jaw-winking reflex, a levator tenotomy is first performed, and later a Reese attachment of the orbicularis to the occipitofrontalis muscle is carried out.

The enlarged epicanthus which occurs in children with bilateral ptosis should not be operated on until the child is older as the condition frequently adjusts itself when the adult facial growth is reached. However, in exceptional cases the Gifford technic is the method of procedure.

I have touched on only the points in treatment of congenital ptosis that seem to me to be most striking and pertinent.

In conclusion, I should like to repeat Dr. Spaeth's closing plea for earlier diagnosis and for as early treatment as is possible in the individual case.

DR. EDMUND B. SPAETH, Philadelphia. The portion of the paper which I could not read because of limitation of time contains a discussion, in very frank detail, of how I feel with regard to various surgical indications and their application. For instance, I do not feel that the occipitofrontalis procedure is permissible except in cases of cicatricial ptosis in adults or of cicatricial ptosis in children with complete paralysis of the levator muscle.

The jaw-winking reflex has been badly managed by most neurosurgeons. It is unfortunate that patients with this complication reach the neurosurgeons, for they become neurosurgical problems for the rest of their lives. It is a simple procedure to convert this type of ptosis into complete paralysis and then carry on from there by means of Reese's method of attachment of fibers and cicatricial bands from the orbicularis to the occipitofrontalis muscle.

Management of Iridocyclitic Secondary Glaucoma DR F BRUCE FRALICK
and DR JAMES H COOPER and DR RICHARD ARMSTRONG (by invitation),
Ann Arbor, Mich

A survey of 1,282 consecutive cases of iridocyclitis revealed that in 261, or 22 per cent, secondary glaucoma was present or developed while the patient was under observation. The ratio of females to males with glaucoma was approximately 2:1. The highest incidence fell in the sixth decade of life, the mean age was 53 years, the youngest patient was 20 years and the oldest 76 years of age.

The cause of the iridocyclitis associated with glaucoma was not definitely proved in any instance, but in over one half of the cases, a definite focus of infection was found.

Of the 261 eyes that had secondary glaucoma, 69 were treated medically as a primary procedure. This type of treatment was carried out over a sufficient period to make possible evaluation of the results. Administration of miotic drugs was tried in 21 eyes with more or less quiescent iridocyclitis. However, the tension was reduced to normal in only 6 eyes. Homatropine or atropine was used in 46 eyes showing acute or subacute uveitis, with reduction of tension to normal in only 17. The tension of 2 eyes was not made normal with either atropine or pilocarpine.

Paracentesis was performed on 58 eyes showing some degree of active uveitis. It was surprising to find that normal tension was obtained in only 25 eyes without a more radical surgical procedure. In only 6 of these 25 eyes was paracentesis repeated more than once when it was the only operation necessary. This may suggest that some other procedure might better be utilized if paracentesis fails on two occasions.

In a summary of 60 cases in which iridectomy was done as an initial or as a final measure, it was found that in 43, or 71.6 per cent, the operation was successful and in 17, or 28.3 per cent, it failed. On the whole, gratifying results in cases of glaucoma secondary to primary iridocyclitis are obtained with iridectomy when the procedure is indicated because of failure of medical therapy or the conservative method of paracentesis.

A single trephination was done on 15 eyes. The intraocular tension was reduced to normal in 9 of these eyes, and none showed any activation of the iridocyclitis. Trephination was the initial operation in 8 instances, in 4 of which it was successful. The trephine operation had been preceded by single or multiple operations of other types on 5 of the 9 eyes in which it apparently controlled the tension. In 4 instances trephination was preceded by iridectomy and in 1 by paracentesis.

Miscellaneous operations were performed, usually as a last resort, in a number of cases in which the prognosis was very poor or other operations had failed. We were surprised to find 23 successes and 14 failures in this group. Cyclodialysis was done on 18 eyes in a quiescent state, and in 10 eyes the tension was reduced to normal during the period of observation. Two transfixions of the iris for *iris bombé* were successful, and 1 failed. Twelve combined extractions for cataract complicated by iritic glaucoma resulted in normal tension in 9 eyes. Iridencleisis as the primary procedure was successful in 2 eyes and failed in 2 eyes after trephination.

Sixty-seven eyes of this series were enucleated. The condition of 35 was hopeless, and enucleation was the primary procedure. Eight other eyes were considered hopeless, but at the request of the patients, medical therapy was tried, without success, for a short period before enucleation. On the remaining 24 eyes one or more surgical procedures were carried out before the condition was given up as hopeless.

DISCUSSION

DR PETER KRONFELD, Chicago. One of the many annoying and exasperating features of iridocyclitic secondary glaucoma is the extreme variability and irregularity of the disease. If in a case of iridocyclitis the intraocular pressure becomes elevated, it is difficult to predict whether this condition will be just a brief episode

or whether it will prove to be permanent secondary glaucoma, resistant to all forms of medical and surgical therapy at one's disposal. Even the gonioscopic findings do not always enable one to tell with certainty whether the anatomic alterations in the angle of the anterior chambers are such that the function of the normal channels of outflow is permanently or irreparably impaired. Thus, in cases of iridocyclitic secondary glaucoma one has to act from day to day, or rather from week to week, since with the one exception of seclusion of the pupils with *iris bombé*, no situation associated with iridocyclitic glaucoma calls for immediate surgical action. The well known tolerance of the human eye to such elevations of intraocular pressure and the possibility that nature will come to one's help justify the conservative attitude which is so well expressed by the term "sitting tight."

I have seen several cases of more or less quiescent iridocyclitis in which an elevation of intraocular pressure, despite intensive medical treatment, persisted for as long as eight months and then subsided, with hardly any permanent loss of visual function. The experiences of my associates and myself at the Illinois Eye and Ear Infirmary are in agreement with those of Dr. Fralick. In treatment of glaucoma associated with quiescent iridocyclitis, cyclodialysis has in our hands scored more successes than a trephine operation. The difference, however, is not great enough to permit the statement that cyclodialysis is the most suitable operation for this type of glaucoma, nor do we have any data, gonioscopic or clinical, which enable us to tell beforehand which of the two operations, trephination or cyclodialysis, is more likely to be successful in a given case.

In a case of extensive peripheral anterior synechia, especially in the upper portion of the angle, I prefer cyclodialysis to trephination.

In each of Dr. Fralick's series of 5 cases cyclodialysis after iridectomy was successful. I wonder whether he attaches any significance to this observation. Was the cyclodialysis made in the area of the coloboma? If so, the success of these operations may have been due to the effect of the iridectomy combined with the cyclodialysis, the procedure advocated by Czermak, Wootton and Wheeler, and recently by Goldmann and Bangerter. In Dr. Fralick's series, iridectomy alone made an unusually good showing. I wonder if extensive posterior synechiae were characteristic of the cases in which iridectomy alone controlled the glaucoma.

I should like to take issue with one point in this paper, namely, the use of the word "only" in the following sentence: "Paracentesis was performed on 58 eyes showing some degree of active uveitis. I was surprised to find that in only 25 eyes was normal tension obtained without a more radical operation." Does such a percentage of successes in a procedure as simple and harmless as paracentesis justify the use of the word "only," when a much more extensive operation, such as trephination, was successful in 60 per cent?

Dr. Fralick's experience that paracentesis repeated several times at short intervals does not tend to be any more effective than one or two paracenteses agrees entirely with ours. It is possible, therefore, that paracentesis acts largely by breaking a vicious circle. Our experience with the cyclodiathermy of Vogt is sufficiently encouraging to warrant recommendation of its trial when other surgical procedures have failed.

The period of postoperative observation in our cases has not been long enough to warrant my presenting any results.

In my opinion, Dr. Fralick and his associates have made a contribution of great practical value in a field where every bit of guidance and advice is keenly appreciated.

DR. F. BRUCE FRALICK, Ann Arbor, Mich. Dr. Kronfeld asked whether the cyclodialysis opening was made in the region of the coloboma of the previous iridectomy. I cannot answer that question definitely, but it is my impression that the opening was not uniformly made in the region of the coloboma but was more commonly placed in the outer lower quadrant.

Dr Kronfeld also raises the question whether posterior synechiae were not common in the cases in which iridectomy was performed. It is true that the patients requiring iridectomy, or on whom iridectomy was done, did show a high percentage of relatively advanced posterior synechiae, and that fact may logically be an explanation for the high percentage of good results in that group. However, this group did not show the characteristics of *iris bombé*, so that the end result would be that of a transfixion.

We also have been favorably impressed by the results of cyclodiathermy cauterization in treatment of the quiescent form of iridocyclitic secondary glaucoma. I have, however, not used it on eyes with good vision. Most of the patients operated on by this procedure have been persons who did not respond to the other forms of treatment, and thus cyclodiathermy cautery was selected as a last resort. We have been favorably impressed with the results in this particular group and may later gain sufficient courage to extend the use of the operation to the patients with less hopeless conditions.

Postoperative Exotropia with Limitation of Adduction. Results of Transplantation of Tenon's Capsule. DR CONRAD BERENS and DR HUNTER H. ROMAINE (by invitation), New York

The technic of obtaining a suitable Tenon capsule graft to be placed between the muscle and the scleral adhesions, although described in a previous publication (*Am J Ophth* 21: 536, 1938), will be discussed in the light of added operative experience.

In the case of a patient operated on by one of us (C. B.) the first operation was a failure, and the operation had to be repeated for postoperative exotropia following reimplacement. This was done, with an excellent result, after consultation with Dr Kirby and Dr White. In another case the exotropia was worse after transplantation of the capsule, the unfavorable result seemed to be due to a reaction to buried catgut. The results in the other cases in which one of us (C. B.) operated were fair to good. In the majority of cases one or more operations had been performed to correct the secondary deviation before Tenon's capsule was transplanted.

In cases of postoperative exotropia, after the muscle is freed from underlying adhesions, it has usually been found advisable to resect a piece of the muscle and advance it about 1 mm anterior to the original insertion. The results are not ideal, and better methods of handling the Tenon capsule graft to prevent reformation of adhesions between the muscle and the sclera may be devised, or other material, which will increase the effectiveness of the operation, may be found which will prove more satisfactory.

We have performed experimental studies on rabbits directed toward improving technic, clarifying clinical findings and possibly obtaining a better substance for the graft.

Patients with postoperative exotropia (caused by adhesions) are so disfigured that any operation which offers hope for improvement seems worthy of trial, especially in view of the generally unsatisfactory results of conventional operations.

DISCUSSION

DR A. D. PRANGEN, Rochester, Minn. This paper by Dr Berens and Dr Romaine is a valuable contribution to surgery of the extraocular muscles. First, it offers a new and feasible method of dealing with postoperative adhesions which interfere with mobility. Second, and of most interest to me, it points to the significance of Tenon's capsule and the value of preservation of its function when operations are performed on the extraocular muscles.

I agree with the conclusions of the authors that the sliding flap, or, better, the apron flap, is the best procedure. By this method less tissue is damaged, fewer sutures are used, and the exposed muscle is enclosed by its original loose

fascial envelope, through which it can slide. The results of this operation, as reported in this paper, are not striking but are encouraging. When cases of limited postoperative mobility due to adhesions are encountered, this procedure should be tried.

In cases of limited postoperative mobility from adhesions, one wonders why such complications occur. I believe they are caused either by unnecessary damage to Tenon's capsule at the time of operation or by the surgeon's overdoing the original operation. The latter cause is obvious and, I assume, does not explain the postoperative cicatricial loss of mobility considered in this paper. The first cause, disturbed function of Tenon's capsule, is the point under discussion. Throughout the years I have watched operations on the muscles, my own work and that of others, and I gradually have come to feel that coarse carpentry will not suffice for the delicate mechanism of the extraocular muscles. The regional anatomy and physiology of the several tissues involved in the function of the extraocular muscles must be understood and respected. Of these tissues, the fascia bulbi, or Tenon's capsule, is of paramount importance. My consciousness of the importance of this capsule was awakened by the late Dr. P. C. Jameson.

The studies on the anatomy and physiology of Tenon's capsule of rabbit eyes made by Dr. Berens and his associates are most informative. They remind one that Tenon's capsule is a sheet of loose fibrous connective tissue enveloping the muscles, a synovial membrane through which the muscles slide. The authors state: "It is significant to note that by even slight manipulation of the muscle, such as would be made in the usual resection or recession, numerous adhesions were produced without the aid of other implements." Postoperatively, every rabbit's eye showed adhesions of the muscle to the sclera, but these adhesions were less between Tenon's capsule and the sclera than between other tissues and the sclera. Moreover, even when the capsule was adherent to the conjunctiva and the sclera, the loose structure of the capsule allowed the muscle to slip through it.

It is clear, therefore, that in operating on the extraocular muscles the surgeon should seek to effect minimal trauma to the portion of Tenon's capsule on the muscle proper and should try to keep the fascial envelope of the muscle intact during resection or recession. With care, this is possible. When the conjunctiva is opened, Tenon's capsule on the muscle can be avoided. When the tendon and muscle are isolated, sharp cutting dissection parallel to the muscle, instead of tearing blunt dissection, can be used. The latter method tends to pull the capsule off the tendon and muscle, particularly if the capsule has been opened by the incision. The tongue of tendon and muscle with the intact capsule then can be altered *en masse*. This, as Dr. Berens and Dr. Romaine have shown, invites fewer scleral adhesions, and, even though adhesions occur, the muscle will slide through its original capsule. I know this to be true from my own experience. It is the reason for my rejection of any operation which advocates destruction of Tenon's capsule in an attempt to improve or preserve mobility. As a further means of lessening the trauma of tissue and adhesions, I have come to use as few tendon sutures as possible and to employ fine no. 000 and no. 0000 plain gut sutures, which cause less reaction but hold long enough for union to occur. Also, I avoid burying these sutures by tying the knots outside the conjunctiva.

For cicatricial loss of mobility I believe the operation, as advocated by Dr. Berens and his associates, is feasible and, as I said previously, should be tried. No doubt, for the reasons already stated, Tenon's capsule is the tissue of choice for correction of these adhesions when a transplant is needed.

DR. CONRAD BERENS, New York. First, permit me to thank Dr. Prangen for his excellent discussion and for his stressing of the importance of preservation of Tenon's capsule in the ordinary, everyday operations on the muscles that the surgeon has to perform. His method of operation is one which I have tried to follow for some time, but I confess that since postoperative cicatricial strabismus occurred in 1 case of mine, I have been doubly careful.

Dr Prangen asked whether we were describing the ordinary overcorrection I have had, and have reported, many overcorrections but not I am glad to say, this type of deviation, in which we found the extensive adhesions between the muscle and the eyeball, with almost complete limitation of movement in the field of action of the affected muscle. One case of cicatricial strabismus is a low incidence in view of the fact that in the early days I was taught to cut into the capsule and to snip along the sclera and that I did it rather freely. In the light of the experiments on animals that my colleagues and I have performed, I do not see why I have not had a great many more of these unfortunate complications.

Results of Irradiation of Malignant Melanoma of the Uveal Tract DR FRANK E BURCH, St Paul, and DR WALTER E CAMP, Minneapolis

The statement has often been made that irradiation of malignant melanomas of the uveal tract is useless. No conclusive proof has accumulated to commend or to condemn this form of therapy as a means of "sterilization" or of destruction of the neoplasm, preliminary to enucleation. The employment of radium after enucleation is frequent when it is available, the idea being that it may prevent local recurrence or metastasis.

In order to afford some evidence of the efficacy of cross fire irradiation of the globe and orbit, as well as the changes in the melanoma produced thereby, sections of irradiated ocular melanomas were studied and compared with similar tumors not so treated. This study seemed worth while, in view of the impossibility of one's determining the degree of malignancy by biopsy, by cytologic study or by the presence and degree of argyrophilic fibers or, in most instances, by predetermination of the probable age of the tumor at the time of the first diagnosis.

No attempts were made to destroy the tumor by application of radium, although several patients in this series refused enucleation until glaucoma, orbital extension or metastases developed. With 1 patient whose affected eye was the only useful one, cross fire irradiation and application of radon were employed, and for a time growth was retarded. Glaucoma subsequently necessitated enucleation.

Our purpose in employing cross fire irradiation under highly competent direction was to determine the possibility of one's safeguarding the patient against local or systemic recurrence.

The results prove that malignant melanoma is not arrested by therapy preliminary to enucleation, that malignant melanoma of the uveal tract is radioresistant to a dose which may be safely employed, and moreover, that although follow-up evidence as to rapidity of metastatic recurrence in the liver, lungs or other organs is difficult to obtain, the mortality rate may be increased by preliminary irradiation, a possibility which is to be considered.

DISCUSSION

DR A B REESE, New York. The authors speak of the poorer prognosis for malignant melanoma elsewhere in the body than for that in the eye. They cite Bloodgood's figures of only 15 per cent of cures in 200 cases of malignant melanoma in other parts of the body, as compared with the approximately 50 per cent of cures in cases of intraocular malignant melanoma. This discrepancy is due not to the difference in location of the same tumor but to the fact that two different tumors are called by the same name. Malignant melanoma in other organs of the body differs from intraocular melanoma not only in regard to prognosis but in regard to its clinical and histologic characteristics. The one seems to be neurogenic and the other ectodermal in origin.

It seems to me the only factor common to these two tumors is the occurrence of pigment. In 39 of the authors' cases glaucoma was present, and in 12 of these the diagnosis of malignant melanoma was not made until the globes were opened in the laboratory, 2 being phthisical. This is not an uncommon experience. It

emphasizes, therefore, the possibility that an eye with long-standing glaucoma may harbor a malignant melanoma, and it serves as another reason for the enucleation of such eyes

Sometimes statements are perpetuated in the literature without any proved scientific basis or without sufficient data. Such has been the case with regard to the effects of irradiation on intraocular malignant melanoma. Dr. Burch and Dr. Camp now give accurate information indicating that irradiation of such a tumor is without benefit in arresting the growth, preventing metastasis or prolonging life. They admit that a longer period of observation would be advisable. Although their observations are negative, it is important to have them established in the literature on a sound basis.

Angiomatosis Retinae Report of Successful Treatment of One Case Dr. PHILIP MERIWETHER LEWIS, Memphis, Tenn.

This paper was published in the August 1943 issue of the ARCHIVES, page 250

DISCUSSION

DR. LAWRENCE T. POST, St. Louis. Dr. Lewis is to be congratulated on the successful treatment of the local ocular manifestation of this rare disease. Though the destruction of one lesion in a case of this disease, in which there may be multiple lesions, may only postpone the evil day, as the author has pointed out, it is to be hailed as a great achievement and might under more favorable conditions, prolong useful vision for many years.

The desirability of the addition to the literature of new cases of this rare disease is a point well taken. It requires a long time for the clinical picture of an unusual condition to become so familiar to all members of the medical profession that they will be on the alert to recognize the signs when encountered. Probably this disease is not so rare as has been thought.

I am reporting 3 cases here, 2 of which I am sure have not been described in the literature, and Dr. R. H. Boots, former resident at Washington University School of Medicine, has encountered 3 other cases in the examination of draftees at Jefferson Barracks in the first six months of his service. I shall now show photographs of 1 of Dr. Boot's patients. It is obvious that when a case of a disease has once been seen and recognized, new cases of a similar nature are much more likely to be identified.

The first case that I shall describe is that of E. C. R., a married woman aged 30 of Dallas, Texas, who was referred by Dr. J. Guy Jones on April 19, 1937. She gave a history of dimness of vision in the right eye of four months' duration. Vision was 20/24 in the right eye and 20/15 in the left eye.

Just temporal to the right macula there was an area of healed inflammation or hemorrhage, measuring 1 disk diameter horizontally by 0.5 disk diameter vertically, over which the retina was somewhat elevated. The descending temporal vein was dilated to about twice its normal size. The accompanying artery was beaded for a distance of 4 disk diameters below the disk and then showed aneurysmal dilatation to about twice its previous size. It could not be differentiated from the vein. The artery and the vein terminated in a silvery gray mass, which was elevated 5 or 6 D. At the apex of the mass was an orange ball, into which the artery and vein led directly. The top of the mass measured 6 D. The disk was somewhat blurred and showed hyperghosis. The cup was filled with new connective tissue, and all veins were dilated. There were a few hyaloid areas in the lower portion of the periphery. Examination of the left eye revealed a normal macula.

Complete examination was not possible, as the patient was making hurried rounds of the country to find some one who could help her. The correct diagnosis of the condition had been made by the referring ophthalmologist. The patient brought excellent illustrations of her fundi, both of which were extensively involved with characteristic vascular lesions and multiple "bee's nest" tumors and the

retina of the right eye was widely detached. I advised her that radium or high voltage roentgen radiation offered the best means of therapy that I knew. Her next stop was to be in Kansas City, where she was to see Dr. Curran. Whether her case has been recorded previously I do not know. An interesting feature of the case was that a brother whom I did not see, was similarly affected. His case was described in a letter to me by Dr. J. Guy Jones. Their father had one blind eye with a white pupil. I wrote her a month ago to find out what had happened since I saw her but the letter was returned unclaimed.

My second case was that of E. D., referred by Dr. Boots from the St. Louis induction center (slide). The greatly enlarged artery and its accompanying giant vein can be well seen. In this case there were no tumors visible and no evidence of cerebellar or other involvement, hence the diagnosis is presumptive. No treatment was given.

The third case was that of B. K., a single woman aged 27, whom I first saw on May 16, 1942. She complained of decreasing vision in her better eye over a period of two weeks. The other eye had always been defective and on examination proved to be moderately amblyopic, with vision of 20/50 and relative central scotoma. This fact, naturally, was an ever present threat to any contemplated therapy.

Vision of the left eye, which contained the angiomatous tumor, was 20/30 (slide). Obviously, the lesion was all in the extreme posterior pole of the eye near the disk and macula, which fact also influenced therapeutic considerations. Edema and exudate had already extended into the macula, involvement of which caused the blurred vision which the patient complained of.

Three methods of treatment seemed worthy of consideration: application of radium seeds, diathermy puncture and application of thermophore. The preference was in the order named, chiefly because of the inaccessibility of the tumor. An earnest wish not to damage the macula further and not to rupture a large vessel in this, the patient's only eye, was never out of the surgeon's mind.

There was only one week in which the patient was available for treatment, because of her personal affairs. Radium seeds were ordered from New York. As ill luck would have it, they did not arrive as planned. Preparations were made, therefore, to use diathermy, the convenient long curved Gradle needle, devised for detachment of the retina, being chosen. Again, bad luck intervened, and this needle could not be found. Hence, the thermophore was finally used. The awkwardness of the approach through the necessarily inadequate exposure was the real deterrent to the operation. The slide shows the tip employed. I devised this instrument some years ago for treatment of retinal detachments. The elbow at the turn near the point and the size of the shaft, necessary to convey adequate heat to the tip, prevented ready accessibility to the sclera opposite the growth. The eye had to be rotated downward, so that direct vision during application was not possible. Neither could the effect be observed immediately because heating at 160° F., a temperature which will destroy choroid and which it was thought would destroy the tumor, does not produce any immediately observable effect. Therefore, if the application had not been made at the desired point, another trial could not be made immediately. After a prolonged struggle, the point was placed over what was thought to be the correct area, though the attempted scarification of the localized spot had not been satisfactory. The optic nerve could easily be felt, and it was known that the tumor was approximately 4 mm. almost directly above it. What was not realized was the possible rotation of the ball in fixation of the globe. I was chagrined to find on examination of the fundus a few days later, when the great reaction had subsided, that the round white area corresponding to the surface of contact with the thermophore was clearly visible just below and temporal to the macula. No opportunity for a picture to show this offered itself and when the fundus was next seen this white area had entirely disappeared and the condition of the eye seemed the same as before the operation.

Encouraged by Dr. Lewis' success, I may try again, using diathermy, though I hesitate to risk further damage to the macula, which is so near the tumor.

DR JACK S GUYTON, Baltimore I wish briefly to present 2 cases in support of Dr Lewis' conclusions

The first case is that of a 13 year old girl with bilateral angiomas of the retinae. The patient has been followed by Dr F H McGovern, of Danville, Va., during the past year. Under his direction her eyes were first treated by roentgen irradiation. This failed to check progression of the lesions, and during June 1942 he referred her for diathermy operations.

I shall confine myself to the results of operation on the right eye. The corrected vision in the eye prior to operation was 20/15 — 2. The single angioma was localized by flashing the light of an ophthalmoscope on the lesion and marking the point where the light penetrated the sclera. Sixteen Walker pins were inserted, as in a detachment operation, into and just around the tumor mass, their position being confirmed by frequent ophthalmoscopic examinations. A current of approximately 15 milliamperes for three seconds was used for each pin. A small hemorrhage appeared within the tumor during this procedure. No attempt was made to close off the nutrient vessels, and at the close of operation the vessels appeared almost as large as before, although the angiomatous mass had been completely obliterated.

Postoperatively, the fundus showed a pronounced reaction. A moderate-sized hemorrhage surrounded the obliterated angioma, and in the overlying vitreous a good deal of subretinal serous exudate was present, producing a flat detachment of the entire upper half of the retina and some subretinal hemorrhage around the temporal side of the disk. This reaction slowly, but completely, subsided. Three weeks after operation the corrected vision was 20/50 — 1. The retinal vessels were gradually reduced to normal size within the first week after operation. Six weeks after operation all hemorrhage and exudate had disappeared, the site of the angioma was a healed scar, and corrected vision had returned to 20/15 — 2.

The second case is that of a 7 year old girl with bilateral juvenile Coats's disease. Progressive failure of vision developed in her left eye during the summer of 1941. She was first examined in September of that year, at which time the left eye was completely blind, with advanced exudative retinitis. This eye was eventually enucleated, after a short episode of secondary glaucoma. Histologic examination showed in the periphery of the retina on one side some unusually large blood vessels associated with an area of massive glial proliferation, and in places a large number of capillaries. There was massive subretinal exudation. There were newly formed vessels on the anterior surface of the iris and ectropion uveae. Although the histologic picture was that of massive exudative retinitis and glial proliferation (Coats's disease), it suggested atypical angiomas of the retinae.

In September 1941 vision in the right eye was 20/20, and the eye was entirely normal except for the fundus. The disk was slightly grayish and definitely blurred. In the far temporal periphery was an area of grayish white exudation, about 2 disk diameters in extent. The vessels over this area were small but showed sharp and irregular changes in direction, as if affected by local elevation of the retina.

During the succeeding months the exudation in the periphery of the right eye gradually increased, also, definite beading of vessels became evident in that region, and a small amount of hemorrhage appeared within the exudate.

During March 1942 the right eye was given 930 r of roentgen radiation in divided doses, a current of 200 kilovolts was employed, with a 2 mm copper and a 1 mm aluminum filter, and with a small aperture to avoid irradiation of the lens. In spite of this therapy, the area of exudation gradually, but steadily, increased, the disk became much more edematous, and a hazy spot of subretinal exudation began to form just below the disk.

The right eye was operated on Aug 1, 1942. The area of exudation in the temporal portion of the periphery was completely obliterated and surrounded with sixteen diathermy punctures, Walker pins being used as in a standard detachment operation. During the first week after operation there was surprisingly little reaction in the fundus. Eleven days after operation corrected vision was still

20/20 — 3 An elevated white area, containing some blood undergoing absorption, extended from 7 to 10 o'clock in the temporal periphery. The disk was slightly more edematous and the subretinal exudate below the disk was slightly more prominent than before operation. Four weeks after operation the reaction in the fundus reached its height, with increased edema of the disk, which extended into the macular region. At this time vision with a pinhole disk was reduced to 20/70. During the succeeding four weeks the area in the periphery that had been treated with diathermy punctures contracted into a white scar with a pigmented border. The edema of the macula and about the disk disappeared, the subretinal exudation just below the disk was absorbed, and corrected vision returned to 20/20 — 3.

There has heretofore been no treatment of any kind for juvenile Coats's disease. The apparent success of diathermy punctures in this case is therefore of considerable importance. There has been a good deal of argument as to whether the pathogenesis of juvenile Coats's disease is the same as, or similar to, that of angiomas retinæ, but whatever the primary cause of the lesion may be, the observations here reported indicate that obliteration with diathermy at least offers a chance of the vision's being saved. It is significant that in this patient eradication of the primary lesion in the periphery of the retina caused disappearance of the edema of the disk and of the subretinal exudation below the disk.

DR. FREDERICK C. CORDES, San Francisco. It is only recently that the treatment of angiomas retinæ has received much attention. In addition to the method employed by Dr. Lewis, radium and roentgen rays have been used. Treacher Collins, in 1930, proposed electrolysis as a possible means of therapy and suggested that localization of the tumor be made according to the methods employed by Gonan. Roentgen radiation has been employed a number of times.

There are few reports of cases in which the patient was observed more than a year. We've reported his results two and a half years after diathermic treatment, and Craig, Wagener and Keenohan published their observations three years after roentgen therapy.

In 1940 Dr. M. J. Hogan and I (Angiomas Retinæ, ARCH. OPHTH. 23: 253 [Feb.] 1940) reported our results in a case of fairly early angiomas retinæ in a woman of 20, who received 1,202 r of roentgen radiation in September 1938. In the left eye a lobulated, reddish yellow mass was situated well out in the periphery below and slightly to the temporal side. The inferior temporal artery a short distance from the disk was greatly dilated and tortuous. In the central portion the artery became sacculated. Accompanying the artery was a tortuous, but more dilated, vein, which started in the mass. There were patches of pale yellow exudate above the macula and a good deal of edema and many linear streaks of exudate along the vessels.

The patient was observed periodically until she moved to Seattle. She retained the improvement described in the paper. In Seattle the patient has been under the observation of Dr. Will Otto Bell, who has kept us informed on the results of her periodic examinations. His letter written three and a half years after the irradiation was started states:

"The sacculatation and tortuosity mentioned in the report have notably receded. The vein remains somewhat enlarged. The mass measures almost 2 disk diameters and is elevated from 3 to 4 D. No other masses have been seen. The patches of pale yellow exudate above the macula mentioned in the original report could not be found, and the linear streaks of exudate above the dilated vein are absent." Vision remains the same as before treatment—0.8 + with correction. Interestingly, this reduction in vision is due to an opacity of the lens that she had before irradiation and which has not increased as a result of the treatment.

My associates and I also have under observation a 14-year-old girl with bilateral angiomas retinæ. The condition is well advanced in the right eye and is in the early stage in the left eye. Her father died at the age of 35 of Lindau's

disease. Aside from the lesions in the eyes, the patient shows no signs of the disease. In February 1941 she received 1,800 r of roentgen radiations to each eye, a dose twice that which Dr Guyton gave his patient. She was last seen in September 1942, two weeks ago, and nineteen months after irradiation was started. The condition in the right eye seems to have definitely progressed. In the left eye the nodule is smaller, white and "harder," as though it consisted for the most part of scar tissue. Vision in the left eye remains at 20/20.

Cases of well advanced disease have been reported in which roentgen therapy was not successful. In our experience this observation seems to be borne out. In the second case the well advanced stage in the right eye showed no regression. The early stage of the disease in case 1 and that in the other eye in case 2 did respond to roentgen therapy, and the eyes have maintained their improvement and function, one for three and a half years and the other for one and a half years.

There still persists a widespread fear of roentgen therapy in treatment of ocular conditions. The most dreaded complication is lenticular opacities, a condition that can be corrected by operation and therefore should not be considered too seriously. Clapp could find only 34 cases of postirradiation cataracts up to and including 1932, a period covering the time when irradiation of an eye was not as well understood as it is now.

On the basis of observation of 3 eyes, 1 of which was irradiated and observed for three and a half years and the other 2 for one and a half years, we feel that in addition to diathermy, roentgen irradiation offers a convenient, safe means of treatment of the lesions of this disease if they are seen early, before gliosis has developed.

DR F. BRUCE FRALICK, Ann Arbor, Mich. I am pleased that Dr. Lewis has again called attention to the fact that angiomas of the retina in some instances is amenable to treatment. He is to be complimented on his careful observations and his results in this case.

It is my belief that the number of patients operated on for this condition will be small and that therefore every surgeon should place on record his results in each operation. I wish, therefore, to report an additional case of angiomas of the retina.

A 26 year old man was referred to me by Dr. Warren B. Dodge, Jr., of Battle Creek, Mich. The patient had experienced no visual complaint until eight months before, when he noted blurred central vision in the right eye. There were no subsequent visual changes and no inflammation. The general health was good, and the family history was without significance. General medical and neurologic examinations revealed a normal status. Vision was 6/30 in the right eye and 6/45 — in the left eye. External and fundic examination of the left eye revealed nothing abnormal. Examination of the right eye revealed normal pressure and no external evidence of disease. Inspection of the fundus of the right eye revealed that the superior temporal artery and vein were much dilated and tortuous. The vessels terminated in an angiomatous cyst in the upper outer periphery of the retina. The superior temporal quadrant of the retina was studded with small lipid flecks. The macular area was infiltrated and edematous and contained many lipid infiltrates. The central field of vision presented a scotoma in the lower mesial quadrant, which included the area of fixation.

On April 29, 1941 a diathermy operation for angiomas of the retina was done according to the method outlined by Herbert Kaye (*Treatment of Angiomas of the Retina*, ARCH. OPHTH. 25:443 [March] 1941). An attempt was made to obliterate the angiomatous retinal cyst with micropuncture pins and to sclerose the superior temporal artery, which supplied the cyst, by diathermic treatment of the scleral surface along the course of the artery. The latter procedure was difficult, since the artery and vein were relatively close together. An attempt was made to produce the fundic picture of arterial, rather than of venous, occlusion.

When the patient was last seen, on Feb 17, 1942, ten months after the operation, vision had improved from 6/30 to 6/15 + in the right eye. The dilated vessels were much smaller than before operation, but the superior temporal artery and vein were still patent. The angiomatous cyst appeared as a productive exudative scar, supplied and drained by the superior temporal vessels. The lipid exudates had nearly all disappeared. The retina was flat, and the hemorrhages had been absorbed, without evidence of their former presence.

This limited experience with a condition for which formerly no therapeutic measure was available offers hope for further improvement in surgical technic and results.

DR ARTHUR J BEDELL, Albany, N Y. I wish to demonstrate by means of colored photographs of the fundus that angiomatosis passes through certain stages whether it is treated or not and, further, that these stages do not fall into definite intervals of time.

(Slide) The first photograph shows an unusually large vein in the inferior portion of the fundus. I believe it is safe to say that when there are very large, parallel blood vessels, angiomatosis is present.

(Slide) The second photograph of the same eye shows the macular exudate and the greater dilatation of both the vein and the accompanying artery.

(Slide) The third photograph, that of the extreme temporal periphery, shows a typical angioma, a rounded, pale, red swelling, with a paler area below and a pinker, upper outer edge, with entering artery and draining vein.

The condition in the second case was in a more advanced stage. The angioma and the blood vessels were small, but the exudate covered a greater area and in the lower part of the fundus the retina was detached. In the case which Dr Lewis presented, retinitis proliferans followed treatment. I am sure that when he reports on the case in another year or two, he will say that the folding and proliferation of the retina have increased.

(Slide) The photograph in the third case exhibits typical changes, with much pigmentation and several retinal ridges.

Angiomatosis is much more common than the reports indicate. I have seen 20 cases and feel certain that others may have been unrecognized.

Why Is a Glaucoma Clinic Desirable? DR HARRY S GRADLE and DR H ISABELLE MCGARRY (by invitation), Chicago.

The glaucoma clinic of the Illinois Eye and Ear Infirmary was established because it was believed that constant supervision of patients suffering from glaucoma would result in a notable decrease in blindness due to that disease. To prove the validity of that belief the following paper presents an analysis of the cases of patients with primary glaucoma who were seen at the clinic during the first year of its existence and who have been under continuous observation ever since. The analysis is based on data on visual acuity, visual fields and tension after six, twelve, eighteen and twenty-four months, as compared with the status of these factors at the time of the patient's admission. The series comprises all cases of primary glaucoma, not merely selected cases, but does not include any case in which the etiologic factors of the hypertension could be proved clinically.

The statistics present evidence that the glaucoma clinic, functioning as a supplement to the regular ophthalmic services of the Illinois Eye and Ear Infirmary, has more than proved its value in the preservation of visual function and in the prevention of blindness in cases of primary glaucoma.

DISCUSSION

DR MARK J SCHOENBLRG, New York. Last year the chairman of the Committee on Glaucoma for greater New York, sponsored by the National Society for the Prevention of Blindness, read before the American Ophthalmological Society a report on a survey of glaucoma records of three ophthalmic clinics in New

York and of one such clinic at Boston. The greater part of this paper illustrated how unsatisfactory and chaotic glaucoma work can be if it is conducted along traditional lines which have remained almost unchanged for the last one hundred years. On the other hand study of the Boston clinic demonstrated that it is not impossible to reform the old ways and that better results are obtainable with more up-to-date methods, just as Dr. Gradle and Dr. McGarity have emphasized in their paper. I wish to add that conditions are improving fast in the ophthalmic clinics of New York.

As an introduction to discussion of the paper, I shall relate some of my own experiences.

In October 1935 my colleagues and I opened a special clinic for patients with glaucoma at the Knapp Memorial Eye Hospital, of New York. The staff of the clinic consisted of a director, an assistant and a medical diagnostician. This group started out with the idea of studying the patients as thoroughly as the means at our disposal would permit. Perimetric measurements were recorded every four to six weeks, the patient's complaints, relating both to the physical and to the mental condition, were entered on the record, no matter how trifling they appeared.

In addition each member of the staff was charged to study and report on a certain phase of glaucoma. Gradually the work branched out in every direction. A social worker and a nurse were added to the staff, and patients were taught how to apply medicaments to their eyes and the elementary rules of personal hygiene and nutrition. The meaning of glaucoma was explained and the importance of cooperation stressed. Printed leaflets containing the necessary information worded in plain language, were distributed among the patients and the members of their families. The clientele of the clinic grew gradually. Thus by organizing a glaucoma clinic, coping with the various practical problems and handling patients in a manner entirely different from the way in which they are being managed in regular clinics, and even in private practice, we learned some things not found in books or in journals. From this experience we reached the following conclusions:

- 1 The glaucoma clinic gives an infinitely better service to patients than the average ophthalmic clinic.

- 2 The clinic offers the attending staff, both medical and nonmedical, the rare opportunity of studying and treating a large number of patients with the same disease within a short time, so that the span of time necessary to acquire a sufficient amount of knowledge about glaucoma is shortened.

- 3 The clinic serves as a center of education for patients and other lay people who are in need of being informed about the prevention of blindness from glaucoma.

- 4 The clinic may serve as a center of education for medical practitioners and others who are the first to come in contact with patients with early glaucoma and on whom we depend for getting such patients.

- 5 It could become a center for research, especially clinical research, on the various phases of the glaucoma problem.

In other words, such a clinic offers (1) better service to patients, (2) an opportunity to the clinician for intensive study of patients with glaucoma, and (3) educational opportunities to both layman and general practitioner. It may also serve as a center for research.

The objections to a glaucoma clinic may be briefly considered. Few ophthalmologists will deny the importance of the organization of special glaucoma clinics. No one could defend successfully the traditional method which has been in vogue for the past century. On the other hand, many ophthalmologists doubt whether the organization of special glaucoma clinics is a practical possibility. Some of their objections refer to (1) the cost of running such a clinic, (2) the lack of medical and nonmedical help, (3) the lack of space, and (4) the opposition of the medical staff of the general ophthalmologic clinic, which does not wish to be deprived of

the experience of seeing patients of this type while a small group of ophthalmologists of the glaucoma clinic "monopolizes" the entire clinical and surgical material of the disease

Those who have condemned innovations in medicine have always been in the majority, and apparently valid objections have always been found even against the most pressing reforms

The shortage of well trained professional perimetrists is indeed a serious problem, but even this can be remedied. Lately, my associates and I have started in New York a course for teaching volunteers the method of perimetry. We hope to have half a dozen perimetrists fairly well trained in about three months. They will then be turned over to a few ophthalmic clinics, where perimetry is done only casually, to work and to continue their training under the supervision of the attending ophthalmologists

A small room 10 by 10 feet (3 by 3 meters) can be fitted out with the necessary implements to serve as a perimetry room. In view of the benefit to be derived from perimetry, the salary of a professional perimetrist is the best investment an ophthalmic institution can make. If there is money for a laboratory for roentgenography and for departments of orthoptic training and correction of aniseikonia, there must be money for perimetry

The accusation that a separate clinic "monopolizes" the glaucoma material is based on misinformation and misunderstanding. The staff of the glaucoma clinic is to be on a rotating basis. The members are appointed for three, six and nine months on a staggered basis, so that there are always ophthalmologists in charge to teach the newcomers from the general ophthalmic clinic the routine of the work and to continue the tradition of thoroughness established by the director

Time does not permit discussion of the subject in greater detail. Men who have had actual experience with glaucoma clinics should have priority in being heard. The opinions of the colleagues from such institutions as the Illinois Eye and Ear Infirmary, the Massachusetts Eye and Ear Infirmary, the Brooklyn Eye and Ear Hospital and the Long Island College Hospital, as well as my own conclusions, should weigh in the balance against those of men who do not approve of special glaucoma clinics on purely theoretic grounds

Dr. John Evans wrote to me a few days ago as follows: "I can state that there is absolute agreement at the Long Island College Hospital that the patients are getting far better care in the glaucoma clinic than in the general clinic." Dr. Henry Mitchell Smith wrote: "From my experience as director of the special glaucoma clinic at Long Island College Hospital, I am convinced that a special clinic is the only way to handle patients with glaucoma in a busy ophthalmic clinic."

I do not doubt all agree that the real difficulty in running a successful glaucoma clinic lies in the discovery of cases of the disease in the early stages. To do this, the public, the general practitioners and the optometrists must be trained. Research work must be encouraged. The ophthalmologist should not be satisfied simply to prevent blindness from glaucoma. Even 20/100 vision is too low a goal. He should strive to save for his patients normal, or nearly normal, visual acuity and field of vision

This discussion should not be concluded without my pointing out one weakness in the otherwise excellent paper of the essayist, namely, the statement that the glaucoma clinic at the Illinois Eye and Ear Infirmary neither treats the patient nor operates. In other words, the clinic concentrates its entire attention on and limits its activity exclusively to, diagnosis. I believe that it is much better, and to the advantage of the patients and of the personnel of the glaucoma clinic, that the complete work (both diagnostic and therapeutic) be carried out at the glaucoma clinic only. Divided interest and responsibility do not lead to complete efficiency. Perhaps the possibility that members of the staff of general ophthalmic clinics may fear they are being deprived of opportunity for glaucoma surgery has dictated the authors' policy of splitting the work between the two services. How-

ever, this fear is due only to a misunderstanding, since, as I have mentioned, one of the purposes of the glaucoma clinic is to give an opportunity to every man from the general ophthalmic clinic to become proficient in every phase of the glaucoma problem by devoting his time at least for one period, of a number of months, exclusively to the work in the glaucoma clinic. This includes, of course, glaucoma surgery.

Differential Diagnosis of Paresis of the Oblique and of the Superior and Inferior Rectus Muscles DR WILLIAM THORNWALL DAVIS, Washington D C

Bielschowsky stated that "by far the most frequent type of single vertical motor anomaly is trochlear palsy."

The most striking sign of palsy of the oblique extraocular muscles, both superior and inferior, is habitual torticollis. The head is not tilted with palsy of the vertically acting rectus muscles. Until Bielschowsky formulated the diagnostic signs for differentiation of palsy of the superior and inferior rectus muscles and palsy of the oblique muscles, paresis of the vertically acting rectus muscles and that of the oblique muscles frequently were confused.

The outstanding differential diagnostic sign may be stated as follows. With palsy of the right superior oblique or of the left superior rectus muscle, when the patient looks up and to the left, there is a high degree of hyperphoria on the right side, due to overaction of the right inferior oblique muscle. With palsy of the right superior oblique muscle, when the head is tipped to the right shoulder, maximum vertical deviation occurs. When the head is tipped to the left shoulder, there is little or no vertical deviation. With palsy of the right superior rectus muscle, there is no change in the vertical deviation when the head is tipped either to the right or to the left shoulder.

There are other diagnostic signs, which will briefly be discussed, but this phenomenon is the most easily observed and the most important. It requires no paraphernalia for detection.

The same difficulty obtains in differentiation of palsy of the right inferior oblique muscle and palsy of the left inferior rectus muscle. When the eyes are rotated to the left, the right eye turns strongly down and in. This is caused by overaction of the right superior oblique muscle, which is the antagonist of the right inferior oblique muscle.

The simplest and most dependable diagnostic sign is elicited by the subject's tipping the head. When the head is tipped to the right shoulder, the side on which the palsy exists, there will be slight or no vertical deviation of the eyes. When the head is tipped to the left shoulder, the maximum vertical deviation occurs. This is the reverse of that which occurs with palsy of the right superior oblique muscle, with which the maximum vertical deviation occurs when the head is tipped to the side of the lesion. With palsy of the inferior oblique muscle, the maximum deviation occurs when the head is tipped to the side opposite the lesion. If the left inferior rectus muscle is paralyzed, there is no difference in the vertical deviation when the head is tipped to one shoulder or to the other.

DISCUSSION

DR SANFORD R GIFFORD, Chicago. Dr Davis has so well described and demonstrated the principal points in the differential diagnosis of palsies of the extraocular muscles that there is little left to say. There should be no need to insist here on the value of exact diagnosis in cases of paralysis of the vertical and oblique muscles. One still sees, however, a number of patients whose disorder has not been diagnosed or, if diagnosed, no provision has been made for appropriate remedial measures. This is a pity, since few patients present more satisfactory results of appropriate surgical treatment than those with partial

paralysis of a vertical or an oblique muscle. The proof of the diagnosis is in the surgical result, and few patients are more grateful than those who have received appreciable improvement in their binocular field, with relief of long-standing discomfort. Most ophthalmologists are similar in an intractable tendency to forget rules concerning paralytic squint. To have forgotten some of them has been more profitable than to have learned them, for it is true that the textbook picture of diplopia, as shown in nine neat little squares, is rarely met with in practice. It is seen only in cases of fresh paralysis and is supplanted rapidly by the complex resulting from contracture or spasm of the opposing muscle. Dr. Davis has done well to describe this stage of paralysis of the superior oblique muscle, in which the diplopia is not limited to the lower and inner part of the field, but exists all over the field and the prominent feature is the upshoot of the paralyzed eye in adduction, due to overaction of the inferior oblique muscle. I should go further and say that this is the usual picture and is common in cases in which the superior oblique muscle has so far recovered as to render difficult the demonstration of any limitation of motion downward and inward.

(Slide) This slide illustrates a case of paralysis of the left superior oblique muscle with typical tilting of the head to the right. The eyes are about level.

(Slide) This slide shows the patient looking up to the right, with overaction of the left inferior oblique muscle.

More practical than the remembering of rules, at least in my experience, has been a somewhat childish method by which the position and functions of the various muscles are visualized while one is looking at the patient. Before the field of diplopia is examined, the deviations in various parts of the field in the cover test are noted as advocated by Bielschowsky, Duane and White, including observation while the head is tipped. Thus, with the action of each muscle in mind, one identifies the muscle which must be paralyzed or overactive in order that the deviation observed may be produced. The only rules worth one's remembering are that in the cover test the deviation of the nonparalyzed eye is always greater than that of the paralyzed eye and that a decided increase in deviation when the head is forcibly tilted nearly always means paralysis of an oblique muscle. I should add one more, namely, that the deviation is always greater in adduction in the case of paralysis of an oblique muscle and is always greater in abduction in the case of paralysis of a vertical rectus muscle.

Bielschowsky's priceless advice is always remembered, namely, that in cases of vertical deviation one should consider only the primary actions of the muscles, as their secondary actions may be neutralized by preexisting phorias. I dislike to think how many diagnoses I have missed by following the textbook picture, which indicated that paralysis of an oblique muscle should result in homonymous diplopia because of the abducting action of that muscle. Almost as often as not, in cases of acquired paralysis, a preexisting exophoria causes the diplopia to be crossed or crossed in one field and homonymous in another. In cases of congenital paralysis of the trochlear nerve convergence is more likely to develop, this may be pronounced enough to stimulate concomitant convergent squint, with overaction of an inferior oblique muscle. This is especially likely to occur when some degree of suppression has developed, as may happen in cases of congenital paralysis, so that diplopia is not noticed. In a child old enough to cooperate, however, diplopia can nearly always be elicited during tests, and in smaller children tilting of the head will always suggest congenital paralysis of the trochlear nerve. The case of a patient with paralysis of the left trochlear nerve whom I recently treated is typical (slide). At the age of 14 years she suppressed the image of the left eye so much that she never complained of diplopia. She was more comfortable, however, when she tipped the head to the right shoulder, and diplopia could be elicited easily when attention was directed to it. In this case the upshoot of the left eye on adduction was the prominent feature, but there was hyperopia in the left eye of 15 prisms in the primary position. (In the picture, she is looking down and in, so that she shows limitation of the motion of the superior oblique muscle

also, but a marked upshoot was evident on her looking straight to the right) The hyperphoria of the left eye has been reduced to 3 prism diopters by excision of part of the left inferior oblique muscle

I have cared for a few patients with congenital paralysis of the trochlear nerve in whom the convergent deviation had become so marked as to require surgical correction, in addition to what was necessary for the vertical deviation. In such cases myectomy of the inferior oblique muscle is usually performed first and is followed later by whatever procedure on the horizontal rectus muscles is indicated by the degree of squint.

As Dr. Davis has pointed out, the most difficult problem of diagnosis is differentiation of partial paralysis of the superior oblique muscle and that of the superior rectus muscle of the opposite eye. This is especially true when there is alternating fixation or fixation with the paralyzed eye. The relative positions of the double images are the same in the two conditions. Thus, with paralysis of the left trochlear nerve there is hypertropia of the left eye, which increases on the patient's looking to the right, with the upper pole of the left image tipped to the right. With paralysis of the right superior rectus muscle, there is hypotropia on the right side or hypertropia on the left side, which increases on the patient's looking to the right, with the upper pole of the right image tipped to the left, though usually only slightly. If the patient fixes with the right, or parietic, eye, the image of the fixing eye is seen as erect, and that of the left eye is tipped, with its upper pole to the right. Usually the head tilting test, as described, reveals notable increase in deviation when the head is tipped to the left side in cases of paralysis of the left trochlear nerve, while the degree of deviation is unchanged, or is decreased, in cases of paralysis of the right superior rectus muscle.

(Slide) This slide illustrates another case of paralysis of the left superior oblique muscle, with the head tilted to the right in the normal position and no deviation.

(Slide) An attempt is being made to force the patient's head to the left, the left eye deviates upward when the patient looks to the right with the head tilted.

When there is doubt, it is often of value to note the degree of deviation of each eye in the cover test. In a recent case of paralysis of the right superior rectus muscle when the patient fixed with the left eye deviation was slight, while when he fixed with the right eye, as shown in the slide, the left eye showed a marked upshoot under cover. This, of course, established the right eye as the paralyzed one. Fortunately, myectomy of the left inferior oblique, which is indicated in cases of paralysis of the right superior rectus muscle, is of almost equal value in cases of paralysis of the left trochlear nerve, with overaction of the left inferior oblique, so one may be wrong in the diagnosis and still do the patient some good.

When one is examining for diplopia, which is seldom done until a tentative diagnosis by means of the cover test has been made, the value of the horizontal line should be emphasized. The images of the vertical line, usually employed, often overlap in such a way as to be fused by the patient. Images of the horizontal line, when tipped, are fused much less easily, and hence the patient will give much more reliable answers as to the tipping of images. Its only disadvantage is the necessity of the patient's mentally rotating the tipped image 90 degrees in order to visualize the rotation of the eye.

(Slide) This slide shows a picture of Bielschowsky's, illustrating paralysis of the left superior rectus muscle and the corresponding fields. The patient is fixing with the parietic eye, and the marked upshoot of the nonparietic eye during fixation with the parietic eye is shown. The next picture shows him fixing with the nonparalyzed eye with little deviation. The next shows the normal movement of the right eye on his looking up and to the right, and the last, the marked limitation of motion of the right eye on his looking up and to the right.

(Slide) This picture shows the horizontal line as it is used, and the next, the mental rotation of the image which one must make in order to visualize rotation

with the paralyzed muscle, which accounts for the tipping. The tipping, of course, is always in the direction in which the paralyzed muscle should move the eye, so that when the left image is tipped with the upper pole to the right, as in this case, there must be paralysis of a right rotator muscle—in this case, the left superior oblique muscle.

(Slide) Once the trick of mental rotation of the image is learned, its advantage is obvious. Many persons will give no information relative to tipping with the vertical line, but do so readily with the horizontal line. The red glass is seldom necessary in such tests, and its use serves only to conceal the deviations which are occurring and which one wishes to observe.

A few slides illustrate this test.

(Slide) This picture was taken in a case of paralysis of the left superior oblique muscle before operation, with a crude picture of the field of diplopia (slide), and the next picture shows the binocular field after myectomy of the left inferior oblique.

(Slide) The next slide shows paralysis of the left superior rectus muscle. When the patient is looking up and to the right, one does not see any deviation. When she is looking up and to the left, there is marked limitation of movement of the right eye in the field of the paralyzed left superior rectus muscle.

(Slide) The next slide (from Bielschowsky) shows paralysis of the inferior oblique muscle. The motion of the left eye is normal when the patient looks up and to the left, but there is complete paralysis of the left inferior oblique when he looks up and to the right.

(Slide) The next slide is a case of mine, one portion of which shows paralysis of the left inferior oblique muscle.

Fixational Corneal Light Reflexes as an Aid in Binocular Investigation

MAJOR EMANUEL KRIMSKY, Medical Corps Army of the United States

This paper appears on page 505 of this issue.

Correlation of the Phenomena of Crossed and Obliquely Crossed Cylinders with Cylinder Retinoscopy and Clinical Refraction

DR CHARLES HYMES, Minneapolis

Crossed and obliquely crossed cylinders may be resolved into spherocylindrical equivalents, which may be determined clinically or by means of precise mathematical formulas. The phenomenon of obliquely crossed cylinders is the basis for cylinder retinoscopy, as well as for the technic of determination of the axis of an astigmatic eye by means of the crossed cylinder.

The only other function of the crossed cylinder in the technic of refraction is that of determination of the power of the cylinder, based on a comparison of diffusion images.

There is no physiologic basis for the use of the crossed cylinder in the determination of the power of the spherical addition for presbyopia.

DISCUSSION

DR W. HOWARD MORRISON, Omaha. This paper contains too much detail in physiologic optics for one to absorb it readily. Most will benefit by reading and analyzing this contribution after it is printed in the Transactions.

In discussing the simple cylinder, Dr Hymes uses the formula $F = \frac{\text{No. of Degrees} \times \text{Power of Lens}}{90}$. This formula, according to Cowan (Refraction of the

Eye, Philadelphia, Lea & Febiger, 1938, p. 250), is not exactly correct. It is, however, easy to remember and to use. To be exact it should read as follows: $D_m = D_c \sin^2 a$ in which D_m indicates power in any chosen meridian, D_c , total cylinder power and a , angle between the axis meridian and the chosen meridian.

Dr Hymes states that as a technic cylinder retinoscopy is not generally used I should say, rather, that cylinder retinoscopy is employed by most refractionists who use the retinoscope expertly

Some attention must be paid to the sphere when the cross cylinder is used to determine the strength of the cylinder. He who uses the cross cylinder finds that he cannot increase the amount of the cylinder indefinitely without decreasing the spherical strength. Conversely, he cannot greatly reduce the strength of the cylinder without increasing the amount of the sphere. This means that the cross cylinder is not used in determining the sphere alone, as stated by some refractionists, but it implies that each time more or less strength of cylinder is indicated by the cross cylinder a spherocylindric change must be made.

Cowan also stated (page 268) that with a cross cylinder

We are able to add either positive or negative cylindric power and at the same time reduce the spheric power in the same denomination and in the same proportionate strength. This differs from the use of plane cylinders for the same purpose.

When making such spherocylindric changes, one must understand the means of obtaining a spherical equivalent, that is, the spherical equivalent of a simple cylinder is equal to one-half the power of the cylinder. For example, the spherical equivalent of a $+4.00$ D cylinder is a $+2.00$ D sphere, or that of a -5.00 D cylinder is a -2.50 D sphere.

The spherical equivalent of a compound is determined by adding one-half the power of the cylinder to the spherical element of the compound. For example the spherical equivalent of $+2.00$ D sph \ominus $+4.00$ D cyl, ax 90 is a $+4.00$ D sphere, that of -2.00 D sph \ominus -4.00 D cyl, ax 180, a -4.00 D sphere, and that of $+3.75$ D sph \ominus -4.00 D cyl, ax 180, a $+1.75$ D sphere.

The refractionist employing the 0.25 D cross cylinder uses his knowledge of the spherical equivalent in this manner. If in a combination of $+3.00$ D sph \ominus $+2.00$ D cyl, ax 90, the cross cylinder indicates less strength of cylinder, the next step is to reduce the cylinder by 0.25 D, it being borne in mind that in reality the sphere has been increased 0.125 D. If the cross cylinder again demands that the cylinder be decreased by 0.25 D, then not only is the cylinder again reduced, but the sphere also is altered. The new lens combination then is $+3.25$ D sph \ominus $+1.50$ D cyl, ax 90. One half of the amount the cylinder has been reduced has been added to the sphere.

Prangen (Some Problems and Procedures in Refraction, ARCH OPHTH 18 432 [Sept] 1937) stated

When it is used for strength the cross-cylinder alters both the sphere and the cylinder, and this alteration should be visualized. If the cylindric effect alone is thought of and the cylinder is changed without the sphere being checked, an increasingly distorted image will be produced, and the interval of Sturm will be exaggerated instead of corrected.

Prangen credited J. C. Copeland, of the Riggs Optical Company, with calling to his attention the rule of spherical and spherocylindric equivalents.

I have had no experience with obtaining by means of cross cylinders the spherical addition necessary for correction of presbyopia. I do, however, understand that some men, particularly optometrists, use a grid chart of horizontal and vertical lines placed at the reading distance and by means of a pair of cross cylinders balance the horizontal and vertical lines with respect to blackness by adding or decreasing spheres in the trial frame. A cross cylinder is placed before each eye with the minus axis at 90 degrees, if the patient with presbyopia needs more correction, the vertical lines will be blacker. Less sphere is indicated if the horizontal lines appear blacker.

DR CHARLES HYMES, Minneapolis. Several points in Dr Morrison's discussion of my paper need to be cleared up. He believes that cylinder retinoscopy is employed by most refractionists who use the retinoscope expertly. This does not indicate whether or not that group comprises a majority of refractionists.

Such a recent text as Maxwell's (Maxwell, J. T. Outline of Ocular Refraction, Omaha, Medical Publishing Company, 1937) states that in cylinder retinoscopy the placing of the correcting cylinder in the wrong axis creates the reflex of mixed astigmatism, which is practically impossible to correct. Maxwell thus inferentially advised against the use of cylinder retinoscopy as a technic. In the body of my paper this very point is discussed both as to its neutralization by means of the correcting cylinder's being shifted toward the true axis of the astigmatism of the eye and as to its actual measurement by means of minus sphere and plus cylinder.

Dr. Morrison apparently confused the clinical spherocylindric equivalents (plural) discussed by Prangen with the geometric spherocylindric equivalent of obliquely crossed cylinders which is the basis of my paper. Prangen's spherocylindric equivalents are equivalents of a sphere and cylinder and not of obliquely crossed cylinders. In the example cited by him in his fine article and cited by Dr. Morrison, he gave ten different formulas for the writing of what he referred to as an "equivalent prescription." After stating that the full correction of the astigmatism would be ideal, Prangen stated that it is often necessary to give the eye a compromise image or partial correction for the astigmatism by partial obliteration of the interval of Sturm. It is these compromise corrections which he referred to as spherocylindric equivalents, which should be tried before eyes which reject full correction because previously glasses had not been worn. Any one of several of these compromise formulas may be equally acceptable to the same eye.

Perhaps the similarity in terminology was the confusing element, but it is well to emphasize that there can be but one answer to a geometric problem not several.

I have but one more suggestion to make regarding the use of the cross cylinder in determination of the correctness of the sphere or the spherical addition for presbyopia, that is, cross cylinders refract rays as cylinders, and not as sphere and cylinder. Thus, the combination of -50 D sph $+100$ D cyl ax 90 refracts rays as a cross cylinder, the -50 D sphere diverges rays at all meridians, and the superimposed $+100$ D cylinder, axis 90 converges all horizontal rays to an equal distance in front of the original point of focus. Thus, only the vertical rays continue to be dispersed by the -50 D sphere. In other words the function of the minus sphere has been changed to that of a minus cylinder. One cannot employ a simple cylinder to test the accuracy of a sphere.

Book Reviews

The Art of Seeing By Aldous Huxley Price \$2 50 Pp 143 New York
Harper & Brothers, 1943

(Reprinted from *British Medical Journal*)

Aldous Huxley had bilateral keratitis at the age of 16 which left him with greatly reduced vision. As is common in such cases, his sight improved towards middle life. After he had become an ardent devotee of the Bates method of visual training his vision improved so that it was "twice as good as before." To repay a debt of gratitude to his benefactor and to make his art more widely known, Huxley has ventured into medical literature and written a book—*The Art of Seeing*.

Bates's hypothesis is, of course, well known to the medical profession: visual derangements and refractive errors are due to a deformation of the eyeball by a condition of nervous and muscular strain in the extra-ocular muscles, for this reason, according to Bates, the refraction may change "a dozen times or more in a second," if a child tells a lie, and so on. According to Huxley "disappointed love" can produce refractive errors, and myopia in children, while it may be influenced by physical factors, is essentially due to the fact that school children "are often bored and sometimes frightened" so that they emerge from the educational ordeal with myopia or some other defect of vision. The universal treatment in all cases is the induction of cerebral and ocular "dynamic relaxation," on the achievement of which the eye becomes normal. This desirable condition is attained by exercises which include palming (covering the closed eyes with the palms of the hands and imagining a beautiful scene), butterfly blinks, relaxed breathing, sunning ("letting go and thinking looseness" and turning the eyes to the sun), swinging (rhythmic swaying of the body while looking out of a window to make the mind "friendly to movement" and "soothe" it "as do the movements of the cradle"), nose-writing (writing with an imaginary pencil attached to the end of the nose), flashing with dominoes, shifting, rubbing and kneading the upper part of the nape of the neck, and a host of other procedures which Huxley admits are undignified but which he assures us permanently help the vision.

Whatever be the value of the exercises, it is quite unintelligent of Huxley to have confused their advocacy with so many misstatements regarding known scientific facts. It has been shown that the hypothesis upon which these methods of treatment are based is wrong, but Huxley, while admitting he is ignorant of the matter and unqualified to speak, contends that this is of no importance because the method works in practice and gives good results, it comes into the category of "art," not of "science." This argument is perfectly allowable, for in other spheres than medicine empirical methods have often produced effective results the rationale of which may be mysterious. The most stupid feature about his book, however, is that he insists throughout on the physiological mechanism whereby these exercises are supposed to work. It would at least have been logical if he had continued to allow the reader to assume that he was speaking in ignorance of anything except results. He only borders on the ridiculous when he says that these methods result indirectly in the relief or cure of many serious diseases of the eyes, such as glaucoma, cataract, iritis, or detachment of the retina, because they "reduce nervous muscular tension, increase the circulation and bring back the *vis medicatrix naturae* to its normal potency." Like the bone-setter who treats by forcible manipulation every joint whether rheumatic or tuberculous, or most obsessionists who believe that every virtue resides in one particular drug or practice, he treats all visual troubles as one all-embracing unity, all amenable to one sovereign remedy.

There is, of course, another side to the argument. There would appear to be no doubt that these exercises have done Aldous Huxley himself a great deal of

good. Every ophthalmologist knows that they have made quite a number of people with a similar functional affliction happy. And every ophthalmologist equally knows that his consulting-room has long been haunted by people whom they have not helped at all. Huxley is quite right when he says that there is a tendency for the ordinary person, when there is a falling-off in vision, to "hurry off to the nearest spectacle shop" and there get fitted for a pair of glasses by some one who has "no knowledge of him as a physical organism or as a human individual." Nothing could be worse medicine than the indiscriminate and mechanical prescription of spectacles. He is quite right in saying that visual disabilities are often muscular and often psychopathic in origin. But every competent ophthalmologist treats the former with curative exercises (of a more scientific type than those recommended here), and, in the second case, at the least should advise the patient of the origin of his difficulties and suggest steps for their amelioration. For the simple neurotic who has abundance of time to play with, Huxley's antics of palming, shifting, flashing, and the rest are probably as good treatment as any other system of Yoga or Coué-ism. To these the book may be of value. It is hardly possible that it will impress any one endowed with common sense and a critical faculty. It may be dangerous in the hands of the impressionable who happen to suffer from glaucoma or detachment of the retina, and undoubtedly will be dangerous in the hands of the anxious parent of a myopic child who may be misled into neglecting the fundamental medical problems of growth, constitution, endocrinology, and rational ocular care, and may be persuaded to subject it to dangerous eye-strain in the absence of spectacles. But the greatest value of the book will be to the psychiatrist as an intimate and revealing self-study in psychology.

STEWART DUKE-ELDER

Transactions of the American Ophthalmological Society. Seventy-Eighth Annual Meeting. Volume 40. Pp 568. Philadelphia. American Ophthalmological Society, 1942.

These transactions present a stately volume of the twenty-three papers read at the annual meeting, Hot Springs, Va., June 1 to 3, 1942, under the presidency of the late Dr. Allen Greenwood. Among the subjects and authors may be mentioned "Practical Importance of Aniseikonia," Dr. Edward Jackson, "A Reply to Criticisms of Aniseikonia," Dr. Walter B. Lancaster, "The Effect of Mydriatics on the Intraocular Pressure in So-Called Primary Wide Angle Glaucoma," Drs. Peter C. Kionfeld, H. Isabelle McGarry and Homer E. Smith, "Some Observations on the Results of Desensitization in Tuberculous Iritis," Drs. E. V. L. Brown, Ernest E. Irons and S. L. Rosenthal, "Experimental Studies in Ocular Tuberculosis," Drs. Alan C. Woods and Earl L. Buiky, "Allergic Keratoconjunctivitis," Drs. C. S. O'Brien and J. H. Allen, "Corneal Vascularization Problems," Drs. Derrick Vail and K. W. Ascher, "Local Sulfonamide Therapy Catarrhal Conjunctivitis," Drs. Phillips Thygeson and Alson E. Braley, "Pre-cancerous Melanosis and Malignant Melanoma of the Conjunctiva and Skin of the Lids," Dr. Algernon B. Reese, "A Colored Reflex from the Anterior Capsule of the Lens Which Occurs in Mercurialism," Dr. Walter S. Atkinson, "Fibroblastic Overgrowth of Persistent Tunica Vasculosa Lentis in Infants Born Prematurely," Dr. T. L. Terry, and "Studies of the Fields of Vision in Cases of Rathke Pouch Tumors," Drs. Henry P. Wagener and J. Grafton Love. Some of these articles were also published in the ARCHIVES.

The volume concludes with the theses of the newly elected members. "Progressive Myopia. A Possible Etiologic Factor," Dr. Edwin W. Burton, "Endophthalmitis with Secondary Glaucoma Accompanying Absorption of the Crystalline

Lens," Dr Robert H Courtney, "Further Observations on Autofunduscopy (Auto-Ophthalmoscopy of Eber, Purkinje Figure of Walker)," Dr Leslie C Drews, "Herpes Zoster Ophthalmicus Report of Cases and Review of the Literature," Dr Ambrose Earl Edgerton, "The Ocular Pathology of Methyl Alcohol Poisoning," Dr Walter H Fink, "Transscleral Lacrimal Canaliculus Transplants," Dr Glen Gregory Gibson, "An Experimental Study of Iridodialysis," Dr George L Kilgore, "The Use of Conjunctival Flap in Cataract Extraction," Dr Walter Moehle, and "Objective Strabismometry in Young Children" Dr Maynard C Wheeler

The new editor of the transactions, Dr Wilfred E Fry, is to be complimented on the excellent appearance of this volume

ARNOLD KNAPP

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PERIPHERAL RETINAL HOLES WITHOUT DETACHMENT

ARNOLD KNAPP, M D

NEW YORK

In the following 5 cases, holes in the periphery of the retina were observed without detachment. I am purposely leaving out of this consideration cases of macular holes, as these have a different causation and a different course. The importance of retinal holes in the causation of retinal detachment is generally accepted, therefore I may be justified in reporting these cases to illustrate that retinal holes may occur without detachment.

CASE 1—J R M, a woman aged 61, complained on Aug 26, 1908 that the sight in the left eye had become clouded ten days previously. There were present fine opacities of the vitreous and some edema of the retina in the nasal periphery, but no detachment. There was an irregular hole of about disk size just below the horizontal meridian in the nasal periphery in which the choroidal vessels could be distinctly observed. At the margin the retina appeared brownish, possibly because of choroidal pigmentation. On Jan 9, 1909, four months later, the edema and the hole in the retina were unchanged. The patient was then lost sight of.

CASE 2—G G, a woman aged 53, had an intracapsular extraction done on the right eye on April 12, 1928. There were no complications, and normal vision was obtained. On March 28, 1935 the patient complained that a shadow had been present before the right eye for one week. Vision with glasses was 20/20—. In the upper and outer periphery the retina was grayish, and a definite hole was present, but no detachment. This hole, about $\frac{1}{8}$ disk diameter, was round, with grayish margins and a lid hanging down like a flap. It was directly next to one of the larger vessels. There was no detachment. The patient was observed at regular intervals and when she was last seen, on May 19, 1942, seven years after the onset of the difficulty, the corrected vision in the right eye was 20/20, there had been no change in the retina or in the hole and there was no ophthalmoscopic evidence of choroidal changes.

CASE 3—M J F, a woman aged 60, complained on Dec 2, 1937 of a sudden obscuration of the right eye, when she was examined the following day the vision with a correction of -6.00 D sph $\subset -4.50$ D cyl, axis 180 was 20/200. There was a field defect in the lower and inner quadrant. There was a considerable number of opacities from blood in the vitreous. On December 6 the vision had improved, the field was less contracted and the fundus was clearer. A semicircular hole, about $\frac{1}{4}$ disk diameter, with a wrinkled margin above, could be distinctly seen in the retina at 11 o'clock. The patient was treated with rest, subconjunctival injections of saline solution and administration of vitamin C. When she was seen on Jan 8, 1942 the vision with glasses was 20/30. There were a few opacities of the vitreous. The retina was unchanged. In the upper and outer periphery of the retina there was the same semicircular hole with a flap at the upper margin, and a little beyond it was a second and much smaller linear hole. The entire area was outlined by a crescentic choroidal pigmented line. The condition was unchanged when the patient was last seen, on Feb 15, 1943.

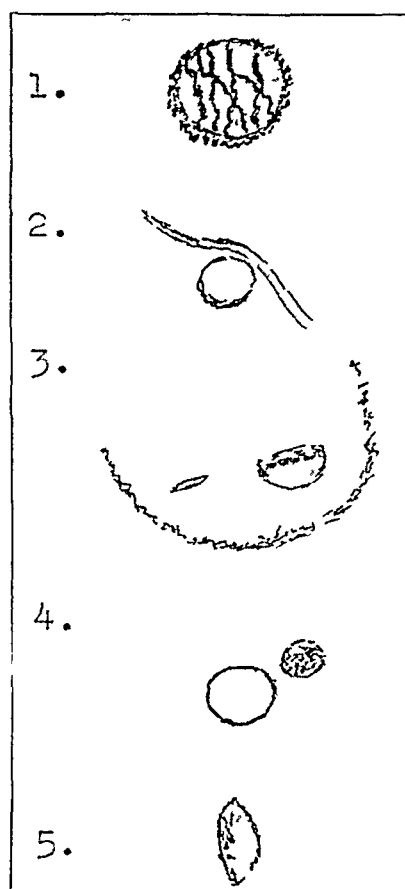
CASE 4—R W B, a man aged 67, complained on June 25, 1942 that the sight of the left eye had been blurred for four days. The vision was 20/50. There were diffuse opacities of the vitreous (blood), and up and out at 2 o'clock there was a definite round hole of about $\frac{1}{4}$ disk diameter, with a separated flap like a lid suspended a little anteriorly in the vitreous. There was no detachment. No change had occurred when the patient died three months later from heart disease.

CASE 5—A J, a woman aged 40, was seen on July 6, 1929 with a history of failure of vision of the left eye for three days. The vision with a correction of -5.50 D sph $\subset 1.00$ D cyl,

Read before the Section of Ophthalmology, New York Academy of Medicine, April 19, 1943

was 60 was 20/30. There were recent opacities of the vitreous (blood), and at about 1 o'clock there was a vertical oval hole with a grayish opacity at the nasal margin like a wrinkled flap. There was no detachment. The right eye was blind from an old detachment. On Oct 10 1929, the vision of the left eye with glasses was 20/30. The vitreous was clear. The hole in the retina could be easily seen, and one margin protruded into the vitreous. There were no choroidal changes. On Jan 9, 1930, six months after the onset of the trouble, the vision became worse, a detachment was definitely present, surrounding the area of the retinal hole in the upper and outer quadrant. The patient was then operated on.

To recapitulate, in case 1 there was a round hole of about 1 disk diameter in the nasal periphery of the retina. The margin of the hole was faintly pigmented, suggesting a chorioretinal adhesion. There was no detachment. The patient was lost sight of after four months. In case 2 a small hole developed in an aphakic eye near a blood vessel in the upper and outer periphery of the



Peripheral retinal holes without detachment (cases 1, 2, 3, 4 and 5)

retina. The margins of the hole were gray and a lidlike flap hung down from above. There was no detachment. This case was observed for seven years. There was no change. In case 3 two retinal holes were present in the upper and temporal periphery of the retina. This area became shut off by a line of choroidal pigmentation. There was no detachment. The case was followed for five years. In case 4 there was a hole in the upper and outer periphery with a stationary operculum but no detachment. This operculum can be explained only by the presence of a detachment of the vitreous. No change occurred, the patient died three months later. In case 5 there was an oval hole in the upper and outer periphery with a wrinkled flap attached to the nasal margin. There was no detachment. Six months later a detachment developed in this part of the fundus. The other eye was blind from an old detachment.

In 3 of these cases the lesion began with a hemorrhage into the vitreous. It is important to remember that hemorrhages into the vitreous in older persons may result from a tear in the retina and are not necessarily due to arteriosclerosis, a fact to which Vogt¹ has drawn attention.

A study of the literature reveals that holes without detachment are not unusual. I have found the following references:

Gonin² stated the belief that certain tears, especially perforations of atrophic origin or more unusually disinsertions, may not always or immediately be followed by a detachment in the surrounding retina.

Arruga³ published drawings illustrating 2 cases in which the tear was surrounded by pigmentation, which indicate a healed inflammatory process and a circular hole with a freely suspended operculum.

Lindner⁴ stated the belief that spontaneous retinal tears without detachment are explained by an adhesion between the retina and the choroid which prevents the development of a retinal detachment.

Vogt⁵ reported 3 cases of traumatic tears at the ora in which the symptoms came on late, and 2 of spontaneous round holes with freely suspended operculums, without detachment.

Sabbatini⁶ reported 5 cases of retinal holes without detachment. About the holes chorioretinitis was present. The margins of the holes were not everted, and there were no signs of traction of the vitreous. In 1 case the hole was seen to heal. The edges lost their grayness, and new choroidal areas developed. The usual subjective symptoms were absent.

Jeandelize and Baudot⁷ on casual examination of the eyegrounds of patients undergoing refraction discovered 3 retinal tears without detachment. One was at the ora. One was in the periphery and was round, with pigment along the macular border. A third was oval and larger than the disk, with exposed choroidal vessels and some pigment along the border.

Burch⁸ reported on an extensive tear in the retina which was under observation for twelve weeks without the development of a retinal detachment. The tear was 2 mm in breadth and extended along the superior temporal vessels 3 disk diameters from the disk to the periphery.

Genet⁹ reported 1 case of a round hole in the retina with choroidal changes after hemorrhage into the vitreous. He said that a hole alone is not sufficient to cause detachment. There must be in addition histologic lesions in the retina, in other words, the retina cannot be sound. Amsler in the discussion said that there must always be changes in the choroid, retina and vitreous to produce a retinal hole.

1 Vogt, A. Photographie einer Bienenwabenmakula bei Retinitis pigmentosa juvenilis, *Klin Monatsbl f Augenh* **102** 519, 1939.

2 Gonin, J. Le décollement de la rétine, Paris, Payot & Cie, 1934, p 77.

3 Arruga, H. Detachment of the Retina, translated by R. Castroviejo, New York, B Westermann, 1936, p 76.

4 Lindner, K. Zur Klinik des Glaskörpers, *Arch f Ophth* **137** 183, 1937.

5 Vogt, A. Die operative Therapie und die Pathogenese der Netzhautablösung, Stuttgart, Ferdinand Enke, 1936, p 123.

6 Sabbatini. Rotture retiniche senza distacco, *Atti Cong Soc oftal ital*, 1935, p 763.

7 Jeandelize, P, and Baudot, R. Aspects de déchirure rétinienne sans décollement appréciable, *Ann d'ocul* **170** 515, 1933.

8 Burch, F E. Extensive Retinal Tear, *Am J Ophth* **21** 669, 1938.

9 Genet, L. Déchirures rétinienne sans décollement, *Bull et mém Soc franç d'opht* **49** 262 1936.

Guillot¹⁰ regularly explored the retinal periphery in all myopes who complained of recent opacities and found several holes without detachment or with limited detachment

Nico Trantas¹¹ wrote that A. Trantas insisted on the existence of retinal holes without detachment in myopic eyes. His 5 cases were insufficiently reported. Mention was made of the importance of examining the periphery of the eyeground with the aid of digital pressure in cases of sudden opacities of the vitreous.

Arruga¹² said that if a detachment does not follow a hole an adhesion of the retina to the choroid must be present to prevent the escape of fluid underneath the retina.

Hanssen,¹³ in a study of the development of detachment in myopic eyes, examined histologically 37 myopic eyeballs without detachment. In 26 there were partial thinning of the retina, cystoid degeneration, slight tears in the inner retinal layers and direct holes. Of the eyes with the changes situated in the anterior part of the eyeball, slight tears were present in 4 and holes in 3, while in the 6 eyes with changes at the equator there were 2 holes. Hanssen regarded the retinal hole as the most important predisposing cause of detachment. He stated the belief, however, that to produce detachment degenerative changes in the vitreous and reduced intraocular pressure must also be present.

These authors explained retinal holes without detachment by the formation of chorioretinal adhesions. While it is clear that an adhesion between the retina and choroid can prevent detachment, choroidal changes were not apparent on ophthalmoscopic examination in 3 of my cases and another explanation should be considered. It may not be out of place to see how these cases fit into the present interpretation of the formation of so-called idiopathic retinal detachment.

Retinal holes without detachment belong to Gonin's second group—round, relatively small holes situated in the equatorial zone or just anterior to it and usually in the lateral or inferior part in a retina which is only slightly raised. This type is due to cystoid degeneration or atrophy of the retina resulting from nutritional disturbances, together with disease of the choroid and deep changes in the vitreous (Amsler and others¹⁴).

In addition, an adhesion of the vitreous to the retina is believed to be present. Adhesions between the hyaloid membrane and the internal limiting membrane occur in every healthy eye, especially at the base of the vitreous. The cause for this adhesion is not known, it is assumed to result from pathologic processes such as degenerative or inflammatory changes in the retina, as had been suggested by histologic examination. In a case of Sourdille's,¹⁵ adhesion of the operculum to the vitreous was present, and the torn-out piece of retina showed inflammatory changes which were believed to explain the adhesion of the vitreous. Vogt⁶ came out definitely with the view that degenerative changes must be present in the

10 Guillot, P. Des déchirures rétiniennes sans décollement, *Bull. et mem. Soc. franç. d'opht.* 48 317, 1935.

11 Trantas, N. Sur l'opération du décollement de la rétine par diathermo-coagulation d'après la méthode de Weve, *Bull. et mem. Soc. franç. d'opht.* 50 234, 1937.

12 Arruga, H. Etiology and Pathogenesis of Retinal Detachment, *Arch. oftal. hispano-am.* 33 312, 1933.

13 Hanssen, R. Zur Entstehung der Netzhautablosung, *Klin. Monatsbl. f. Augenh.* 74 778, 1925, 75 463, 1926.

14 Amsler, M., and others, in Bailliant, P., Coutela, C., Redslob, E., and Velter, E. *Traité d'ophtalmologie*, Paris, Masson & Cie, 1939, vol. 5, p. 525.

15 Sourdille, G. Étude histologique de 2 cas récents de décollement de la rétine, *Cong. Soc. franç. d'opht.*, 1932, p. 236.

retina before a rupture can take place. These changes consist in cystoid degeneration and nutritional disturbances in the retina without involvement of the vitreous. Leber¹⁶ stated the belief, and his views were accepted by Gonn and Lindner, that rupture of the retina occurs at the place where adhesion between the vitreous and the retina has taken place.

Changes in the vitreous are particularly important in the pathogenesis of retinal detachment. It is generally accepted that the vitreous undergoes liquefaction and contraction and that a detachment of the vitreous ensues. Lister¹⁷ stated the belief that detachment of the vitreous is common and is due to actual contraction of the vitreous or its liquefaction. This author suggested that traction of an adhesion between the retina and a contracting vitreous is sufficient to cause a rent. This tearing could be more easily produced on sudden rotation of the eye, especially if the retina was weakened by cystic degeneration. Lindner¹⁸ favored the role of the vitreous in the development of a detachment and said that a posterior detachment of the vitreous is essential. Especially important is the partial fluidification of the vitreous, this makes traction of the vitreous uneven and leads to rupture of the vitreous or retina with escape of fluid from the vitreous. Lindner¹⁹ has examined histologically many eyes with retinal detachment and found that the detached vitreous was adherent to the peripheral margin of the retinal tear and that the subvitreous space and subretinal space were in communication. Sallmann and Rieger²⁰ proved clinically the presence of a detachment of the vitreous in nearly all cases of retinal detachment. The clinical examination was made possible by the use of Lindner's angular microscope and a contact glass. Unfortunately only a part of the fundus about the posterior pole can be examined by this method and a clear vitreous is essential. Sallmann²¹ has demonstrated the frequent presence of a detachment of the vitreous in freshly enucleated eyes. Bock²² was fortunate enough to make a satisfactory examination of the vitreous in 2 cases of retinal detachment before and after operation. In these cases an adhesion between the peripheral margin of the hole and the vitreous was observed and the adhesion persisted after the successful operation. Vogt accepted the statement that detachment of the vitreous is frequently present in cases of detachment of the retina but claimed that it occurs even more frequently without such detachment in senile and myopic eyes and in eyes with senile and presenile destruction of the framework of the vitreous. He had never observed a case of detachment of the vitreous in which a detachment of the retina subsequently appeared.

Best²³ drew attention to the clinical fact that localization of the tear is three times as frequent in the upper part as elsewhere, and the same proportion holds true for the site of detachment. Hence it is clear that gravity must play a definite role and increase the pull of the vitreous.

16 Leber, T, in Graefe, A, and Saemisch, E. T. *Handbuch der gesamten Augenheilkunde*, Berlin, Julius Springer, 1916, vol. 7.

17 Lister, W. Detachment of the Vitreous, *Tr. Internat. Cong. Ophth.*, 1922, p. 63.

18 Lindner, K. Zur Klinik des Glaskorpers, *Arch. f. Ophth.* **137** 158, 1937.

19 Lindner, K. Zur Klinik des Glaskorpers, *Arch. f. Ophth.* **137**-170, 1937.

20 Sallmann, L., and Rieger, H. Ueber hintere Glaskörperabhebung bei Ablatio retinae, *Arch. f. Ophth.* **133** 75, 1934.

21 Sallmann, L. Zur Anatomie der hinteren Glaskörperabhebung, *Arch. f. Ophth.* **135** 593, 1936.

22 Bock, J. Ueber den klinischen Nachweis der Anheftung des Glaskörpers am Rissrand bei Netzhautabhebung, *Arch. f. Ophth.* **140** 468, 1939.

23 Best, F. Zur Pathogenese der Netzhautablosung, *Ber. u. d. Versamml. d. ophth. Gesellsch.* **33** 186, 1906.

The movement of the vitreous is another important factor in the development of a detachment. Best²⁴ has demonstrated that in every movement of the eyeball the vitreous undergoes movement, exerting a pull on the peripheral parts where the hyaloid membrane adjoins the internal limiting membrane of the retina. Lindner²⁵ has particularly emphasized the importance of ocular movements, and his interesting experiments have confirmed Lister's views that the rotating and torsional movements are the more powerful. Vogt²⁶ had also accepted the role of movement of the vitreous in the development of a detachment and mentioned the enormous whirling of the framework in the myopic and senile vitreous when this is examined with the slit lamp microscope. According to Lindner the vitreous pulls on the retina during rotating and whirling movements of the eyeball and causes a rupture just at the margin of the attachment of the vitreous.

The nondevelopment of a retinal detachment may be due to the absence of any one of these factors.

It seems reasonable to assume that in the case of certain types of holes the changes in the retina are a sufficient explanation and that in the case of retinal holes without detachment the changes in the vitreous are not developed to the extent necessary to cause detachment. If one leaves aside the question of adhesion and traction of the vitreous, the fact that a detachment did not occur in the cases described in this article must mean that there was no access to the subvitreous fluid or that if the vitreous was not detached there was no tear in the hyaloid membrane to permit escape of fluid from the vitreous.

When detachment of the vitreous is absent, changes in the texture of the vitreous were assumed by Vogt, such as partial liquefaction with formed vitreous elements, which on whirling movements of the eye traumatize a weakened retina at the site of an adhesion.

As for treatment, the patient naturally should be kept under observation and examined for the presence of a detachment of the vitreous. Amsler²⁷ expressed the opinion that a retinal tear should be operated on even if no detachment has occurred. I agree with Vogt that an operation is not necessary before the detachment develops. At the same time a history of detachment in the other eye is ominous, as in case 5 of my series, and suggests that similar changes probably will occur in the recently affected eye. The operation before the retina becomes detached should be a simple one.

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24 Best, F. Der Glaskörper bei Augenbewegungen, *Klin Monatsbl f Augenh* **42** 538, 1904.

25 Lindner, K. Prevention of Spontaneous Retinal Detachment, *Arch Ophth* **11** 148 (Feb) 1934.

26 Vogt, A. Histologischer Befund eines weiteren Falles von relativ frischer spontaner (senil-myoper) Netzhautablosung, *Monatsbl f Augenh* **98** 735, 1937.

27 Amsler, M. Muss ein Retinariss operiert werden, auch wenn eine Ablatio nicht eingetreten ist? *Klin Monatsbl f Augenh* **101** 920, 1938.

CARBAMINOYLCHOLINE CHLORIDE IN PETROLATUM

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Carbaminoyleholine chloride is a synthetic drug introduced in 1932 as a long-acting substitute for acetylcholine. The drug produces miosis and cyclotonia and decreases intraocular pressure, consequently, it is used as an agent in the treatment of glaucoma. Carbaminoyleholine chloride is poorly absorbed from the conjunctival sac when instilled in simple aqueous solutions, however, O'Brien and Swan¹ found that when precautions were taken to insure absorption, carbaminoyleholine chloride had a more intense and prolonged hypotensive effect on glaucomatous eyes than had corresponding doses of pilocarpine salts. They observed that the addition of a surface tension-reducing agent, zephiran chloride, facilitated penetration of carbaminoyleholine chloride from aqueous solutions into the normal cornea. However, other precautions are necessary to insure absorption. The solution of the drug must be administered so that it covers the cornea, and the lids must be kept closed to maintain good contact between the cornea and the solution for at least several minutes. Massage of the cornea through the lids further enhances absorption. Recent investigations have suggested a simpler and more effective method of administration of the drug.

Swan and White² demonstrated that the physical properties of the drug and the vehicle profoundly affect the rate of penetration of a given drug into the cornea. The relative affinities of the drug for the cornea and for the vehicle are particularly important. Most substances of low surface activity, high affinity for water and low affinity for lipids enter the normal cornea slowly when administered in simple aqueous solutions. When these substances are administered as a suspension in pure olive oil or petrolatum, penetration is rapid. Carbaminoyleholine chloride has the physical properties of this class of substances, consequently, it should be most effectively administered as a suspension in pure oil.

PRESENT STUDY

Experiments were made on the eyes of albino rabbits. Effectiveness of absorption of carbaminoyleholine chloride was judged by the onset, intensity and duration of miosis produced by contact of a given concentration of the drug with the cornea for specific periods. An ointment base of pure petrolatum³ was observed to be a considerably more effective vehicle than zephiran solution (1:3,500) or zephiran jelly (1:2,000) and many times more effective than distilled water. The addition of hydrous wool fat to the petrolatum resulted in decreased absorption, probably because the hydrous wool fat contained sufficient water to retain the hydrophilic

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1 O'Brien, C. S., and Swan, K. C. Carbaminoyleholine Chloride in the Treatment of Glaucoma Simplex, *Arch. Ophth.* **27**: 253 (Feb.) 1942.

2 Swan, K. C., and White, N. G. Factors Affecting Penetration of Drugs into the Cornea, *Am. J. Ophth.* **25**: 1043, 1942.

3 The consistency of the ointment was adjusted by mixing liquid petrolatum U. S. P. and white petrolatum. A stable and even suspension was readily obtained, as carbaminoyleholine chloride was available in sealed ampules as a fine, dry powder.

carbaminoylcholine in the ointment and to prevent its transmission into the cornea. When the corneal epithelium was removed or damaged, differences in the effectiveness of the various vehicles were reduced greatly.

In clinical experiments the ointment was prescribed in small ophthalmic tubes with pointed tips to facilitate self administration and accurate dosage. Patients were instructed to look into a mirror and squeeze out a quarter of an inch (0.6 cm) of ointment (0.05 cc) onto the conjunctival side of the everted lower lid and then to look down in order to bring the ointment into contact with the cornea. They were advised that temporary blurring of vision occurs as the ointment spreads on the cornea and that this blurring indicates that the ointment is properly applied.

Clinical experiments were made on a group of 15 eyes (9 patients) with chronic noncongestive glaucoma. Pilocarpine administered three to four times daily was ineffective in controlling the tension or in preventing visual loss. Carbaminoylcholine chloride (1.5 per cent in 0.03 per cent solution of zephiran chloride) administered three to four times daily was effective in maintaining the tension below 30 mm mercury (Schiotz) and in preventing loss in the visual fields in 11 of the 15 eyes during periods of five months up to three years. However, carbaminoylcholine chloride (1.5 per cent) in petrolatum administered only twice daily was equally effective in controlling the tension in these 11 eyes. In 2 eyes the tension was not consistently controlled by carbaminoylcholine chloride in solution of zephiran chloride when the drug was administered at home three to four times daily, but administration of the ointment twice daily at home was successful. In the fourteenth and fifteenth eyes, carbaminoylcholine chloride in any vehicle did not effectively control the tension, although miosis (2.5 mm pupil) and spasm of accommodation (0.75 to 2.75 D) were maintained more consistently with the ointment than with zephiran solution or zephiran jelly.

The clinical studies indicated that a suspension of carbaminoylcholine chloride in pure petrolatum was more effective than the same percentage of carbaminoylcholine chloride in solution of zephiran chloride, particularly when applications of the drug were made by the patient or by his family. Only 3 of the 9 patients considered that administration of the ointment was more difficult than that of the carbaminoylcholine chloride-zephiran solution. All found the ointment to be more economical, as less frequent administrations were required.

SUMMARY

Carbaminoylcholine chloride has a high affinity for water and a low affinity for lipids. Like other substances with these properties, it penetrates the normal human and rabbit cornea more readily when administered as a suspension in a pure petrolatum base than when given in simple aqueous solutions, in a solution zephiran chloride or in ointment bases containing hydrous wool fat. In the treatment of chronic noncongestive glaucoma, administration of carbaminoylcholine chloride in petrolatum is more effective and economical than other methods of administration of the drug.

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GUIDES IN THE OPERATIVE (COSMETIC) TREATMENT OF NONACCOMMODATIVE CONCOMITANT SQUINT IN ADULTS

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The question as to how one can be guided in determining the amount of operative correction and the selection of the proper muscles for operation for relief of squint has been raised many times. Many diverse answers have been given. The amount of correction described as obtainable with a measured amount of shortening or lengthening of a specified muscle has varied greatly. So many variable factors were found in the reports that it was felt that a series of operations for squint in which the variables were minimized would give valuable information. Such a series of operations were performed at the Barnes General Hospital during a period of approximately one year.

MATERIAL AND METHOD

The group consisted of 65 operations on the internal and external rectus muscles of male Army personnel, ranging in age from 20 to 49 years. All operations were performed by the same surgeon. No patients with pronounced anomalous retinal correspondence, strabismus fixus, accommodative squint or a marked vertical component were included in this series. In addition, a considerable number of men with alternating divergent squint, especially those of the divergence excess type, were excluded because the preoperative deviation under cover varied considerably at different examinations. After operation the angle did not vary, but at times the postoperative deviation was greater than the deviation before operation. Patients of this type should have a period of monocular occlusion before examination. In addition, the cover should not be alternated as rapidly in examination of these patients as in tests on persons with other types of squint.

The angle of squint was measured by the cover test, for both 20 feet (6 meters) and 33 cm, loose prisms being used for all patients with normal fixation in each eye. With the patients whose fixation was eccentric or poor, the perimeter was used for measurement.

Each patient was tested for the possible development of postoperative diplopia due to the presence of pronounced anomalous retinal correspondence before operation by placing the full prismatic correction which was necessary to stop movement of the eye under cover before the uncovered eyes and determining whether diplopia was present. If an annoying diplopia appeared, the probability of such a postoperative condition was explained to the patient. Usually operation was not done under such circumstances.

Only two types of operative procedure, resection and recession, were included in this series, not only because this limitation in the range of operations was desirable but because these two procedures have been adequate in correcting safely practically all types of horizontal strabismus. In some patients with divergent squint, complete tenotomy of one or both external rectus muscles was necessary to obtain parallelism. These patients were not included, however.

The resection operation used was the Lancaster procedure, modified as follows. The conjunctiva was incised vertically in a separate layer just in front of the insertion of the muscle. Tenon's capsule was then incised vertically. The cut edge of the conjunctiva and capsule on the side away from the limbus was lifted so as to expose the muscle and the capsular reflections. The latter were cut as far back as the resection was expected to extend. A Prince forceps was introduced and clamped on the muscle just in front of the measured amount of muscle to be resected. The tendon was then severed just behind its attachment to the sclera. Two double-armed 0000 mild chromic sutures were passed through the stump from within outward. Each was then passed through the muscle just behind the Prince forceps, from within outward, and then tied over the muscle. The forceps was removed.

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and the excess muscle resected Tenon's capsule and the conjunctiva were closed with a continuous silk suture

The recession operation used in this series was the Jameson procedure, modified as follows The conjunctiva was incised vertically in a separate layer just in front of the insertion of the muscle Tenon's capsule was similarly incised, and the cut edge of the capsule and conjunctiva on the side away from the limbus was lifted so as to expose the muscle and the capsular reflections The latter were cut, and a strabismus hook was inserted under the muscle at its attachment A single-armed 0000 chromic catgut suture on an atraumatic needle was whipstitched into each side of the tendon just behind its attachment The hook was removed and the tendon attachment severed, the sutures being used for traction The muscle was then retracted, and the needle of each suture was passed through the superficial layers of the sclera Each suture was then tied separately The conjunctiva and Tenon's capsule were closed with a continuous silk suture

In all the operations local anesthesia was used, both by instillation and by injection A 5 per cent solution of cocaine hydrochloride was used by instillation in six doses of 1 drop each at two minute intervals One-half cubic centimeter of a 2 per cent solution of procaine hydrochloride was injected deep into each muscle to be operated on, so that no conjunctival infiltration occurred A single silk traction suture was placed near the limbus on the side of the muscle to be operated on After operation, binocular occlusion was used for five days with patients both of whose horizontal rectus muscles were operated on or on whom a resection was done and for three days with patients on whom only a recession was performed In all but 1 patient only one eye was operated on at a time Conjunctival sutures were removed on the fifth postoperative day When the reaction had subsided and the eye had paled, measurements of the residual angle of deviation were made in exactly the same manner as that employed in the original examination

AMOUNT OF CORRECTION OBTAINABLE BY OPERATION

Theoretically, 1 mm of movement of the eyeball should move the optic axis 5 degrees of arc This value is based on the fact that the circumference of the eyeball is 72 mm Movement of the insertion of a single muscle 1 mm should result in the optic axis being moved half that amount unless it is balanced by a movement of the antagonistic muscle in the opposite direction to the same degree However, the theoretic degree of correction of a muscle does not agree with that observed in practice, owing to such factors as the fascial attachments, the relative strength of the muscles, the muscle operated on and the convergence-divergence relation In patients with monocular concomitant squint, if one eye is constantly held in one position, either of convergence or of divergence, there is an inhibitional (Chavasse) lack of ability to rotate the eye completely in the opposite direction even if the nonsquinting eye is occluded This defect is innervational and does not represent a true paresis, but it does affect the relative strength of the two muscles

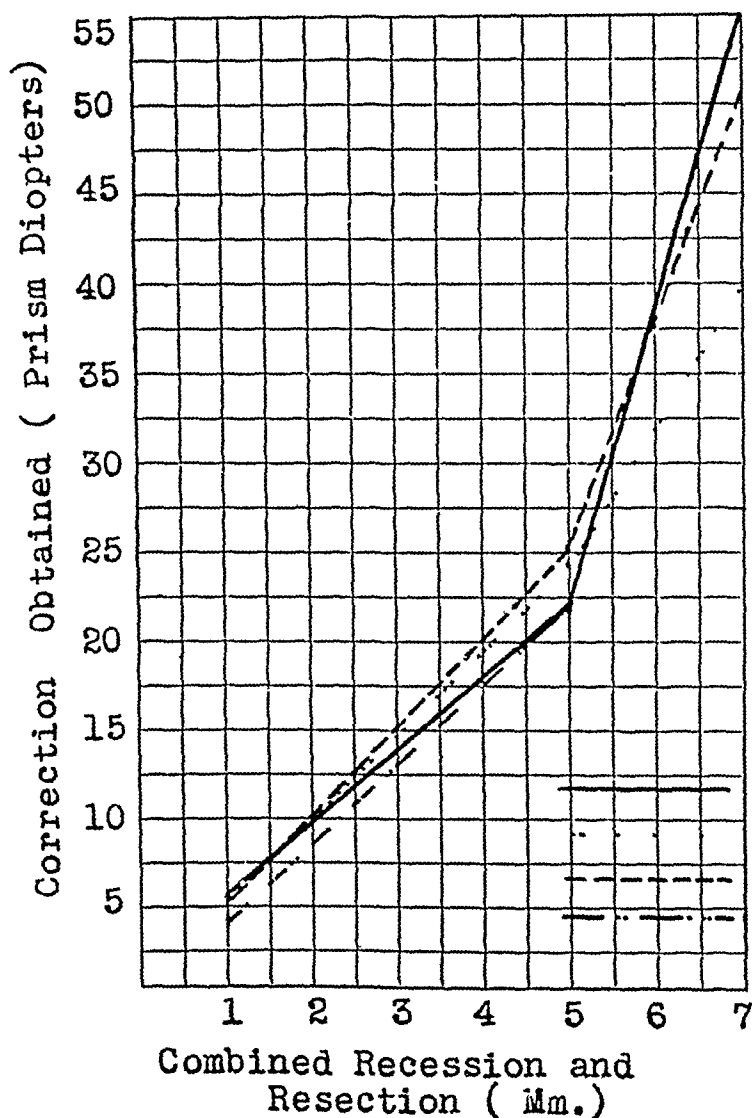
Lancaster¹ pointed out that movement of the insertion of a single muscle 1 mm results in a change of 4 prism diopters of deviation for squints of small degree In a large eye 1 mm of shift of the center of the cornea results in a correction of less than 5 degrees,² while in a smaller eye such a shift results in a correction of more than 5 degrees Wiener and Alvis³ expressed the opinion that 1 mm of change in the muscle insertion results in a change of roughly 10 prism diopters (approximately 5 degrees of change), if balanced by operation on the opposing muscle

1 Lancaster, W B Graduate Lecture read at the meeting of the American Academy of Ophthalmology and Otolaryngology, 1940

2 Lancaster, W B, in Berens, C The Eye and Its Diseases, Philadelphia, W B Saunders Company, 1936, p 1136

3 Wiener, M, and Alvis, B Y Surgery of the Eye, Philadelphia, W B Saunders Company, 1939, p 356

It is obvious that there is a difference in the amount of correction obtained depending on whether the operation is a lengthening or a shortening process and on whether the internal or the external rectus muscle is concerned. Jameson⁴ stated that 1 mm of recession results in 5 degrees of correction if done on the internal rectus muscle and in only 2 degrees of correction if done on the external rectus muscle. In other words, a 5 mm recession of the internus rectus muscle would result in 20 to 25 arc degrees of correction, and a 5 mm recession of the



Graphic representation of the average correction (for a distance of 20 feet [60 cm]) obtainable by combined resection and recession of the horizontal rectus muscles

In this figure, values for alternating convergent strabismus are indicated by a solid line, values for monocular divergent strabismus, by a line of dots, values for monocular convergent strabismus, by a broken line, and values for alternating divergent strabismus, by a line of dots and dashes

externus rectus muscle would give one-third that correction. Worth⁵ stated that 1 mm of recession corrected 4 degrees of deviation if done on the internus rectus muscle and 2 degrees of deviation if done on the externus rectus muscle. Gifford⁶

4 Jameson, P. C. Entity of Muscle Recession, *Arch Ophth* **21** 362 (Feb) 1939

5 Worth, C. *Worth's Squint*, ed 7, edited by F. Bernard Chavasse, Philadelphia, P. Blakiston's Son & Co., 1939, p. 583

6 Gifford, S. R. *A Textbook of Ophthalmology*, Philadelphia, W. B. Saunders Company, 1938, p. 393

expressed the belief that 1 mm of recession corrected 3 degrees of deviation if done on the internus rectus muscle and only 1.5 degrees if done on the externus rectus muscle. According to Peter,⁷ 5 mm of recession in a case of convergent squint corrects 11 to 12 degrees of deviation at the most, and with good technic, a combined recession and advancement may give a net correction of as much as 25 degrees, although in most cases it may be 5 to 7 degrees less.

Dunnington and Wheeler⁸ found that the average correction resulting from a single recession of 4 mm was 7.3 prism diopters. With a simultaneous recession of 4 mm and a resection of 10 mm on the same eye, an average of 40 prism diopters of correction was obtained. Gibson⁹ found that in cases of convergent squint with 10 to 20 degrees of deviation, 4 to 6 mm of correction, divided between the two muscles, was necessary. For a deviation of 25 to 35 degrees he found 6 to 8 mm of total correction to be necessary. For a deviation of 40 to 50 degrees he recommended a total correction of 9 to 10 mm, and for squint of over 50 degrees, a total correction

TABLE 1—*Alternating Convergent Strabismus*

Initials	Age, Yr	Deviation (Esotropia)		Recession of Internal Rectus Muscle, Mm	Resection of External Rectus Muscle, Mm	Residual Deviation (Esotropia)	
		Distant Vision, Δ	Near Vision, Δ			Distant Vision, Δ	Near Vision, Δ
1 O F W	28	45	54	5	7	9	16
2 O F W	28	9	16		4	0	12
3 R A B	20	10	20	5		0	0
4 R H	24	20	20		6	10	10
5 E T C	23	20	20	4	4	0	0
6 O E	20	46	55	5	6	16	23
7 O E	20	16	23	5		10	12
8 C E	20	10	12		5	0	0
9 L A G	24	32	36	5	5	12	12
10 L A G	24	12	12		6	0	0
11 C H	35	33	30	5	5	10	12*
12 E G Z	25	34	34	5	5	8	8†
13 E G Z	25	8	8		3	3	3†
14 E D W	21	16	20	5		4	8
15 E D W	21	4	8	3		5†	0
16 M W H	29	24	18		5	9	9
17 M W H	29	9	9	2		0	0
18 C E G	22	67	67	7	7	12	12
19 O E G	22	12	12	4		0	0

* High plus angle Δ

† Diplopia following orthoptics residual deviation corrected with prism base out

‡ High angle

of 12 mm. He observed that under identical conditions more correction was usually attained by combined recession and resection on one eye than by bilateral recession.

My own results indicate a significant variation in the amount of correction obtainable with the same amount of resection or recession of either of the horizontal rectus muscles. The present series of 65 operations are classified as follows, the average amount of correction obtained for each millimeter, 5 mm and, in combined operations, 7 mm of recession or/and resection being indicated after each type. These values, it should be noted, are not absolute, but have served as excellent guides in successful treatment in subsequent cases.

Convergent Squint—(a) Alternating Type (19 operations, table 1) Each millimeter of recession of the internal rectus muscle resulted in a correction averaging

7 Peter, L. C. Present Status of Tendon Transplantation of the Ocular Muscles, *Am J Surg* 42:30, 1938.

8 Dunnington, J. H., and Wheeler, M. C. Operative Results in Two Hundred and Eleven Cases of Convergent Strabismus, *Arch Ophth* 28:1 (July) 1942.

9 Gibson, G. G. Analysis of Operative Results in Concomitant Strabismus, *Arch Ophth* 23:477 (March) 1940.

2.4 prism diopters for distance and 3 prism diopters for near vision (for 6 recessions of 2 to 5 mm each). A 5 mm recession of the internal rectus muscle alone resulted in a correction averaging 9.3 prism diopters for distance and 14.3 prism diopters for near vision.

Each millimeter of resection of the external rectus muscle resulted in correction averaging 1.9 prism diopters for distance and 1.8 prism diopters for near vision (for 6 resections of 3 to 6 mm). A 5 mm resection of the external rectus muscle alone resulted in a correction averaging 9.5 prism diopters for distance and 10.5 prism diopters for near vision.

Each millimeter of combined recession of the internal rectus muscle and resection of the external rectus muscle (7 operations) resulted in an average correction of 2.8 prism diopters for both distance and near vision (for 4 to 7 mm of correction of each muscle). The correction obtained from a combined 5 mm resection and recession on each muscle averaged 2.3 prism diopters for distance and 2.6 prism

TABLE 2—*Monocular Convergent Strabismus*

Initials	Age, Yr	Deviation (Esotropia)		Recession of Internal Rectus Muscle, Mm	Resection of External Rectus Muscle, Mm	Residual Deviation (Esotropia)	
		Distant Vision	Near Vision			Distant Vision	Near Vision
1 J B L	33	40° *	40°	7	7	15°	15°
2 J B L	33	15°	15°	5	5	0	0
3 R. T	22	30°	28°	5	3	22°	18°
4 R. T	22	22°	18°	5	6	0	0
5 J T M	22	30°	30°	7	8	17°	13°
6 J T M	22	17°	13°	5	5	0	0
7 A O D	21	6Δ	16Δ	5	3	0	3Δ
8 H L S	24	10°	10°	5	5	0	7Δ†
9 F L B	27	36Δ	36Δ	5	5	12Δ	12Δ
10 F L B	27	12Δ	12Δ		5	0	0
11 D W B	24	37Δ	37Δ	5	5	12Δ	12Δ
12 D W B	24	12Δ	16Δ	4		7Δ	6Δ
13 D W B	24	7Δ	6Δ		4	0	0
14 S M S	26	30Δ	26Δ	5		9Δ	9Δ‡
15 R A E	49	65Δ	65Δ	7	7	12Δ	10Δ
16 R A E	49	12Δ	10Δ	5		0	0
17 E H C	25	18Δ	23Δ	5	5	0	0
18 M H F	22	34Δ	38Δ	6	6	4Δ	7Δ
19 M H F	22	4Δ	7Δ	2		3Δ	3Δ
20 M A C	22	25°	25°	7	7	0	0

* Although not strictly accurate, 1 arc degree is taken to be equal to 2 prism diopters.

† Exotropia.

‡ High angle Δ.

diopters for near vision. In a single case a combined 7 mm resection and recession on each muscle resulted in 5.5 prism diopters of correction for both distance and near vision.

(b) *Monocular Type* (20 operations, table 2). Each millimeter of recession of the internal rectus muscle resulted in correction averaging 2.4 prism diopters for distance and 2.5 prism diopters for near vision (for 4 recessions of 2.5 mm). A 5 mm recession of the internal rectus muscle alone resulted in a correction averaging 16.5 prism diopters for distance and 13.5 prism diopters for near vision.

Each millimeter of resection of the external rectus muscle resulted in correction averaging 2.1 prism diopters for distance and 2 prism diopters for near vision (for 2 resections of 4 to 5 mm). A 5 mm resection of the external rectus muscle alone resulted in a correction of 12 prism diopters for both distance and near vision.

Each millimeter of combined recession of the internal rectus muscle and resection of the external rectus muscle (14 operations) resulted in a correction averaging 2.7 prism diopters for distance and 2.8 prism diopters for near vision (for 3 to 7 mm of correction of each muscle). The correction obtained from a combined 5 mm

resection and recession on each muscle averaged 25.1 prism diopters for both distance and near vision. For a combined 7 mm resection and recession on each muscle an average correction of 51 prism diopters for distance and 51.6 prism diopters for near vision was obtained.

Divergent Squint—(a) Alternating Type (17 operations) Each millimeter of recession of the external rectus muscle alone resulted in correction averaging 2.7 prism diopters for both distance and near vision (for 3 recessions of 5 to 7 mm). A 5 mm recession of the external rectus muscle alone resulted in a

TABLE 3—*Alternating Divergent Squint*

Initials	Age, Yr	Deviation (Exotropia)		Recession of Internal Rectus Muscle, Mm	Recession of External Rectus Muscle, Mm	Residual Deviation (Exotropia)	
		Distant Vision, Δ	Near Vision, Δ			Distant Vision, Δ	Near Vision, Δ
1 R T F	24	24	24	5	5	9	10
2 E T	23	30	40		5	14	20
3 E T	23	14	20		5	0	0
4 L O H	26	25	32	5		20	10
5 G J H	22	28	18	6	6	8	4
6 M F K	29	47	49		5	32	33
7 M F K	29	32	33	3		23	23
8 M F K	29	23	23	5	5	7	0
9 O J S	23	60	60	6	5	34	34
10 A E K	27	20	20		6	3	7
11 T A R	22	36	5	7		10	3
12 P H S	24	26	26	7	6	9	0
13 M U	26	25	25	5	5	10	10
14 M U	26	10	10		3	0	0
15 A E A	27	35	35	5	5	6	4
16 J B S	24	35	40	5	5	0	4
17 H R P	21	22	35	5	5	0	2

TABLE 4—*Monocular Divergent Squint*

Initials	Age, Yr	Deviation (Exotropia)		Recession of External Rectus Muscle, Mm	Recession of Internal Rectus Muscle, Mm	Residual Deviation (Exotropia)	
		Distant Vision	Near Vision			Distant Vision	Near Vision
1 R J T	21	12Δ	22Δ	6*		4Δ	0
2 H W W	31	20°	20°	6	6	9°	9°
3 H W W	31	9°	9°		6	4°	3°
4 R C R	26	12°	12°	5	5	0	0
5 E O D	33	25°	25°	6	7	8°	8°
6 E O D	33	8°	8°	3	4	0	0
7 W S	24	65Δ	65Δ	6	6	17Δ	17Δ
8 W S	24	17Δ	17Δ		5	0	0
9 H V M	29	20°	20	7	7	0	0

* Both external recti

correction averaging 10.5 prism diopters for distance and 22.5 prism diopters for near vision.

Each millimeter of resection of the internal rectus muscle alone resulted in correction averaging 3 prism diopters for distance and 3.2 prism diopters for near vision (for 5 resections of 3 to 6 mm). A 5 mm resection of the internal rectus muscle alone resulted in a correction averaging 15 prism diopters for distance and 18.6 prism diopters for near vision.

Each millimeter of combined recession of the external rectus muscle and resection of the internal rectus muscle (9 operations) resulted in a correction averaging 2 prism diopters for distance and 2.1 prism diopters for near vision (for 3 to 7 mm of correction of each muscle). The correction obtained from a combined

5 mm operation on each muscle averaged 23.2 prism diopters for distance and 25.8 prism diopters for near vision

(b) Monocular Type (9 operations) Recession of the external rectus muscle alone resulted in 0.6 prism diopter of correction for distance and 2.2 prism diopters of correction for near vision (for 6 mm resection of each external rectus muscle in 1 case)

Each millimeter of resection of the internal rectus muscle alone resulted in correction averaging 2 prism diopters for distance and 2.6 prism diopters for near

TABLE 5—Summary of Average Corrections Obtainable by Resection and/or Recession of the Horizontal Rectus Muscles

Types of Operation	Convergent Strabismus		Divergent Strabismus	
	Alternating	Monocular	Alternating	Monocular
Recession of internal rectus muscle (alone)				
1 mm	2.4△ distance 3.0△ near vision	2.4△ distance 2.5△ near vision		
5 mm	9.3△ distance 14.3△ near vision	16.5△ distance 13.△ near vision		
Resection of internal rectus muscle (alone)				
1 mm			3.0△ distance 3.2△ near vision	2.0△ distance 2.6△ near vision
5 mm			15.△ distance 18.6△ near vision	17.△ distance 17.△ near vision
Recession of external rectus muscle (alone)				
1 mm			2.7△ distance 2.7△ near vision	0.6△ distance 1.8△ near vision
5 mm			10.5△ distance 22.5△ near vision	
Resection of external rectus muscle (alone)				
1 mm	1.9△ distance 1.8△ near vision	2.1△ distance 2.0△ near vision		
5 mm	9.5△ distance 10.5△ near vision	12.△ distance 12.△ near vision		
Combined operations on external and internal rectus muscles of one eye				
Each 1 mm	2.8△ distance 2.8△ near vision	2.7△ distance 2.8△ near vision	2.0△ distance 2.1△ near vision	2.7△ distance 2.7△ near vision
1 mm both muscles	5.6△ distance 5.6△ near vision	5.4△ distance 5.6△ near vision	4.0△ distance 4.2△ near vision	5.4△ distance 5.4△ near vision
5 mm each muscle	23.△ distance 22.6△ near vision	25.1△ distance 25.1△ near vision	23.2△ distance 25.8△ near vision	24.△ distance 24.△ near vision
7 mm each muscle	55.△ distance 55.△ near vision	51.0△ distance 51.6△ near vision		40.△ distance 40.△ near vision

vision (for 2 resections of 5 to 6 mm) A single 5 mm resection of the internal rectus muscle alone resulted in a correction averaging 17 prism diopters for both distance and near vision

Each millimeter of combined recession of the external rectus muscle and resection of the internal rectus muscle (6 operations) resulted in a correction averaging 2.7 prism diopters for both distance and near vision (for 3 to 7 mm of correction of each muscle) The correction obtained from a single combined 5 mm operation on each muscle was 24 prism diopters for both distance and near vision From a single combined 7 mm operation on each muscle, the correction was 40 prism diopters for both distance and near vision

Comment—From table 5 it is evident that the average values are fairly consistent. Resection of the internal rectus muscle resulted in more correction than did recession of that muscle, while the opposite result was obtained with operation on the external rectus muscle, on which recession was generally more effective. Combined resection and recession resulted in approximately the same amount of correction for all four categories of squint considered. The most interesting result derived from this series of operations is the fact that with an equal resection and recession of 7 mm each the amount of correction was approximately twice that obtained with an equal resection and recession of 5 mm each. This is undoubtedly related to changes in the subsidiary duction action of the superior and inferior rectus muscles. At any rate, it negates any possible consideration of the theoretic value of 5 arc degrees of correction for 1 mm of shift in the optic axis.

It will be noted that recessions of 7 mm were done in some cases in spite of the fact that it is a standard procedure not to do a recession of the internal rectus muscle of more than 5 mm or one of the external rectus muscle of more than 3 mm. Jameson⁴ stated that 1.5 to 2 mm can be added to the recession spaces if the eyeball is large. It has been my feeling that whenever possible correction of the deviation should be divided between the two horizontal muscles of the eye to be operated on and that in cases of large angles of squint, especially of the alternating type, correction of the deviation should be divided between the two eyes. In doing this I have noted less tendency to produce abnormal amounts of traction on one muscle. A recession of 7 mm of either muscle when combined with a 7 mm resection of its opponent did not interfere with the motility of the eye in any case.

Although the values found in this series pertain to adults with nonaccommodative squint, the same values were obtained for a small number of children and for adults with accommodative squint who were operated on during the same period.

To determine whether there is any difference between the correction obtained when one operates on the deviating eye in a case of monocular squint and that obtained when the fixing eye is operated on, the results of operation on patients with monocular squint (tables 2 and 4) who had both eyes operated on (at different times) were compared. For 7 patients with monocular convergent squint the average correction was 2.7 prism diopters for distance and 2.8 prism diopters for near vision for each millimeter of operation on the muscles of the deviating eye and 2.8 prism diopters for distance and 2.6 prism diopters for near vision for each millimeter of correction of the muscles of the nondeviating eye. For 3 patients with monocular divergent squint the average correction was 2.8 prism diopters for distance and near vision for each millimeter of operation on the muscles of the deviating eye and 2.8 prism diopters for distance and 2.4 prism diopters for near vision for each millimeter of operation on muscles of the deviating eye. Thus it appears that there was no difference between the amount of correction obtained from operation on the deviating eye and that obtained from operation on the nondeviating eye in cases of monocular squint.

GUIDES TO THE SELECTION OF THE PROPER MUSCLE FOR OPERATION

In order to choose the proper surgical procedure in cases of concomitant squint, it is important to determine the nature of each case, especially as regards the relative state of convergence and divergence and the angle of deviation for distance and for near vision. With high degrees of deviation equal amounts of recession and resection of the muscles of the deviating eye are indicated, the amount usually being divided between the two eyes if the deviation is over 25 to 30 degrees. This is particularly true in cases of monocular squint in which the visual acuity of the

deviating eye is very low. In these cases the relative near point of convergence is not of as much importance, since the degree of deviation is rather constant for distance and for near vision. With smaller degrees of squint, the relative near point of convergence is of extreme importance and is the deciding factor in the decision as to which muscle or muscles should be operated on. The following plans of treatment are based on these considerations, together with the guiding values as to the amounts of correction obtainable with the operative procedures previously mentioned.

Convergent Squint—When the deviation for near vision is significantly greater than that for distance and the relative convergence near point is close, the deviation is of the convergence excess type. Recession of the internal rectus muscle should be the primary procedure. In cases of monocular squint the deviating eye should be operated on first, while in cases of alternating squint the eye which turns in longest on attempting to converge should be operated on first.

When the deviation for distance is greater than that for near vision and the relative convergence is poor, the deviation is of the convergence insufficiency type. Resection of the external rectus muscle of the deviating eye should be the primary procedure.

Convergence Excess Type For deviations up to 15 prism diopters recession of the internal rectus muscle of the deviating eye is indicated. For deviations of 12 to 25 prism diopters recession of the internal rectus muscle and resection of the external rectus muscle of the deviating eye, in proportions indicated by the values obtained in the first portion of this paper, should be performed.

Convergence Insufficiency Type For deviations up to 16 prism diopters resection of the internal rectus muscle of the deviating eye is indicated. For deviations of 16 to 25 prism diopters resection of both internal rectus muscles or resection of the internal muscle of the deviating eye and recession of the external rectus muscle of the same eye, depending on the deviations for distance and near vision, are indicated.

Deviations above these amounts require combined operations on the deviating eye and later correction of the other eye for the residual deviation.

Divergent Squint—When the deviation for distance is greater than that for near vision, the squint is considered to be of the divergence excess type. Recession of the external rectus muscle of the deviating eye should be the primary operation. When the deviation for distance is less than that for near vision, it is considered to be of the divergence insufficiency type. Resection of the internal rectus muscle is then the primary operation. In cases of alternating squint the eye which turns out first in an attempt to converge should be considered as the deviating eye.

Divergence Excess Type For deviations up to 10 or 11 prism diopters recession of the external rectus muscle of the deviating eye is indicated. For deviations of 10 to 20 prism diopters recession of both external rectus muscles or recession of the external rectus muscle of the deviating eye and resection of the internal rectus muscle of the same eye, depending on the deviations for distance and for near vision, are indicated.

Divergence Insufficiency Type For deviations up to 12 prism diopters resection of the external rectus muscle of the squinting eye is indicated. For deviations of 12 to 20 prism diopters resection of both external rectus muscles is indicated. For deviations of over 20 prism diopters, resection of the external rectus muscle and recession of the internal rectus muscle of the deviating eye, in the proportions indicated, should be done.

In a majority of cases of considerable deviation the measurements for distance and for near vision are the same. Here equal amounts of recession and resection are best. In cases of monocular squint it is my policy to do most, or all, of the correction on the deviating eye, up to 7 mm. of correction on each of the horizontal rectus muscles, and to divide the correction for residual deviation between the horizontal rectus muscles of the other eye.

It must be pointed out that one should not be guided wholly by stereotyped tables, but such data can be of definite help to the beginner. One must determine the type of deviation and its measurement for distance and for near vision, with and without correcting lenses and in the cardinal directions of gaze. In addition, the motility, the convergence ability and the retinal correspondence must be determined in every case in order to make proper use of the guiding principles already indicated.

PUPILLARY REFLEX TO DARKNESS

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AND

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In 1939 one of us (Lowenstein¹) described a pupillary reflex which he called the "reflex to darkness." In order to elicit this reflex both eyes of the subject tested are adapted to a constant level of illumination in which darkness is a periodic stimulus. Two small lamps separated from each other by a screen (so that the right eye cannot see the left lamp and vice versa) burn continuously for a period of twelve minutes, which is the time necessary for adaptation. The light of one or the other of these lamps is periodically interrupted by a motor interrupter for one second². During the test the patient fixes on a nonluminous point in the distance. The resulting movements of the pupils are recorded by pupillography.

The reflex to darkness is manifested both directly and consensually. The pupillographic representation of a normal reflex to darkness is shown schematically in chart 1. The pupils had been adapted to light in the period preceding time *A*. The period of unilateral stimulation by darkness lasts from *A* to *B*. The pupil dilates during this period after a latency period. When at *B* the former level of illumination is restored bilaterally, the pupil responds with a contraction and redilation. The period from *A* to *B* is called the primary reaction, or primary dilation. The period from *B* to *C* is called the secondary reaction and consists of contraction (*c* to *d*) and secondary redilation (*d* to *e*).

Actual records of the reflex to darkness in human beings and animals are shown in figure 2 and figure 5 *A*. Figure 2 shows a reflex to darkness (*III*) compared with the reflexes to light (*I*) and to near and far vision (*II*) in the same subject.

In comparative pupillographic studies it was shown that the reaction to darkness occurs in the monkey, cat, rabbit and pigeon as well as in man. The secondary redilation, however, is fully developed only in man. There are occasional suggestions of a secondary redilation in the monkey, but it is constant only in man.

In man and in all the species of animals examined, a definite relationship can be demonstrated between the magnitude of the reactions to light, to darkness and to near vision. The extent of the contraction in the light reflex is about equal to that produced in the reaction to near vision. The ratio of this contraction to the dilation phase of the reaction to darkness is about 9 to 2 (fig 2). The extent of dilation to darkness in its primary phase is about one half of the extent in diameter of the subsequent contraction when the darkness stimulus has ended. However, a comparison of the latter depth of contraction to that seen in a normal reaction to light shows it to be only about one third as great in extent.

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Pupillographic Studies. IV. From the Neurologic and Ophthalmologic Departments of New York University College of Medicine

1 Lowenstein, O. Les troubles du réflexe pupillaire à la lumière dans les affections syphilitiques du système nerveux central, Paris, Gaston Doin & Cie, 1939

2 Lowenstein, O., and Friedman, E. D. Present State of Pupillography. Its Method and Diagnostic Significance, Arch Ophth 27 969 (May) 1942

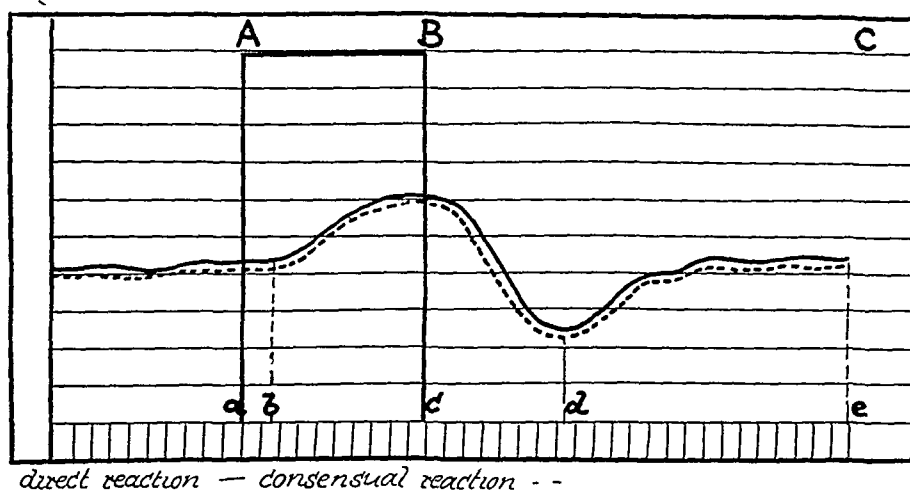


Fig 1—Pupillary reaction to darkness (schematic) The space to the left of *A* represents adaptation to light *A* to *B* represents unilateral stimulation by darkness Both pupils dilate (primary phase of dilation) after a latency period (*a* to *b*) The space on the right to *B* represents the same light conditions as those in effect before use of the darkness stimulus From *c* to *d* is the primary contraction phase (greater than the preceding dilation) and from *d* to *e* the secondary dilation phase

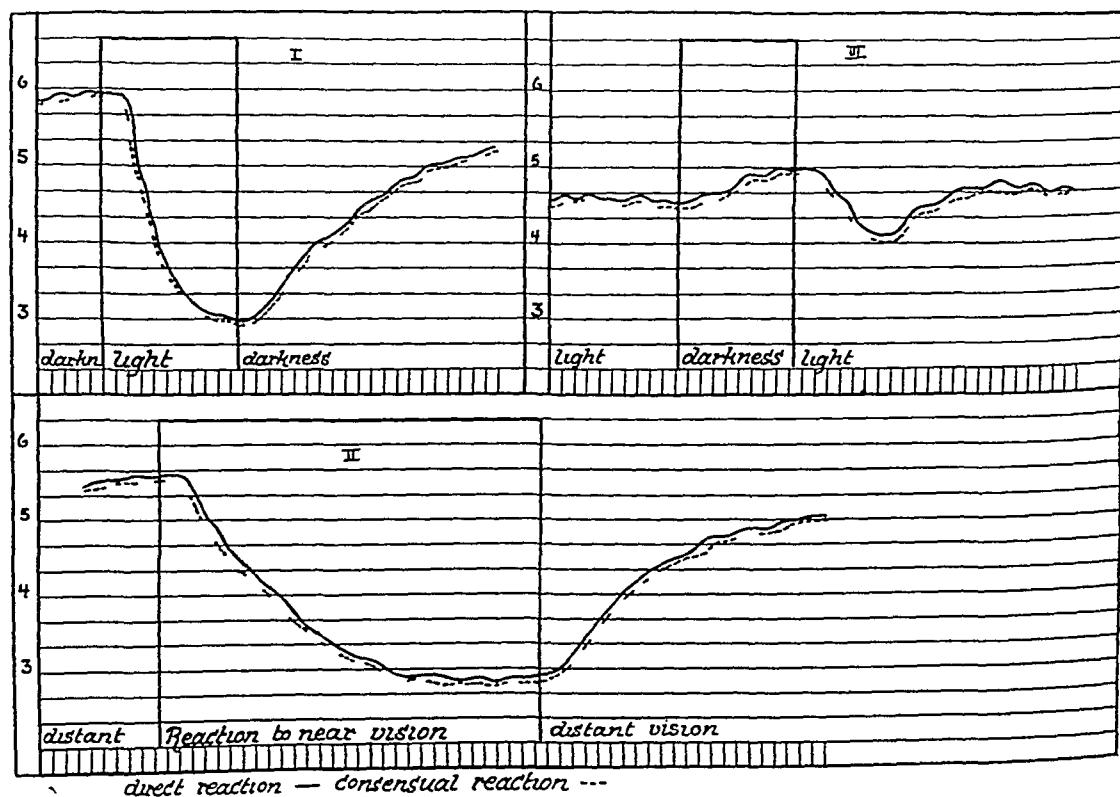


Fig 2—Reflex to darkness (III) as compared with that to light (I) and to near and far vision (II) in the same person

In each species of animals examined there is a characteristic relationship between the change in pupillary diameter in the contraction phase of the light reflex and the dilation phase of the reflex to darkness. In all animals studied so far, the ratio of the darkness reflex to the light reflex was greater than it is in man. It is at its maximum in the cat, in which it may be up to 1 to 1 (fig 3). The extent of pupillary contraction following the dilation to darkness has been about the same as the primary dilation to darkness in all animals examined to date. There is, therefore, no need for a redilation following the contraction. In man, however, since the contraction following the dilation to darkness is greater in extent than the preceding dilation, a secondary dilation has to take place. Secondary redilation exists therefore only in man.

It has long been known that in man the redilation following the contraction to light may under pathologic conditions be absent. The so-called neurotonic pupil, characterized by a good contraction to light which is not followed by an equivalent redilation, has been described in the literature from time to time. It is

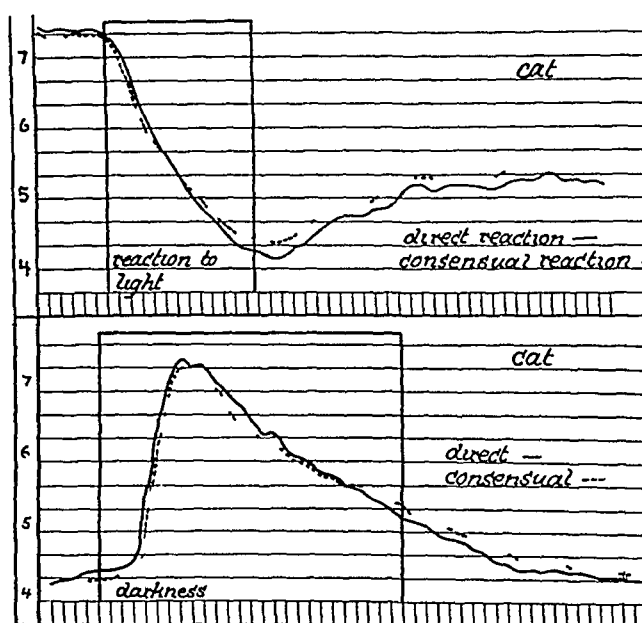


Fig 3—Reflex to light and darkness in a cat. The extent of the dilation to darkness is about the same as that of the contraction to light. (The ratio is generally between 1 to 1 and 1 to 2.)

ordinarily considered to be an infrequent condition. However, in pupillographic examinations it is more frequently found than would be expected.

The first line of figure 4 illustrates the fact that a pupil, although it cannot redilate immediately after a contraction to light, may be able to contract further after a second or a third light stimulus. The picture of "descending pupil" of Lowenstein develops. On the other hand, cases have been noted in which the contraction is rather poor but the redilation is good. After repeated stimulation by light, the pupillary diameter is increased over its original size ("climbing pupil" of Lowenstein). These conditions show that more complex factors are involved in the redilation after contraction to light than simple relaxation within the area of the third cranial nerve. Under pathologic conditions these factors may outweigh the action of the third nerve.

Whereas the reflex to darkness may frequently disappear completely concomitantly with the reflex to light, as with the Argyll Robertson or absolute fixed pupil,

there are cases demonstrating a certain independence of the two reflexes from one another. A case of neurotonic pupil in which the redilation after contraction to light was absent but the primary dilation in the darkness reflex was present has been reported³. Other cases have been observed in which the primary reaction to darkness was absent but the reflex to light was present in both of its phases. Figure 5 shows a graphic summary of some possible modifications of the darkness reflex as it has actually been observed in pathologic conditions. In *A* a normal reflex to darkness is shown. In *B 1* the primary dilation, which is of normal extent, is preceded by a preliminary contraction in a case of anisocoria. In *B 2* the primary dilation is absent, while secondary contraction and redilation are normal. In *B 3* the secondary phase is absent in the reaction of the directly stimulated pupil but present in the consensually reacting pupil. In *B 4* the secondary dilation phase is absent, while primary dilation and subsequent contraction are present. *B 3* and *B 4* show anisocoria.

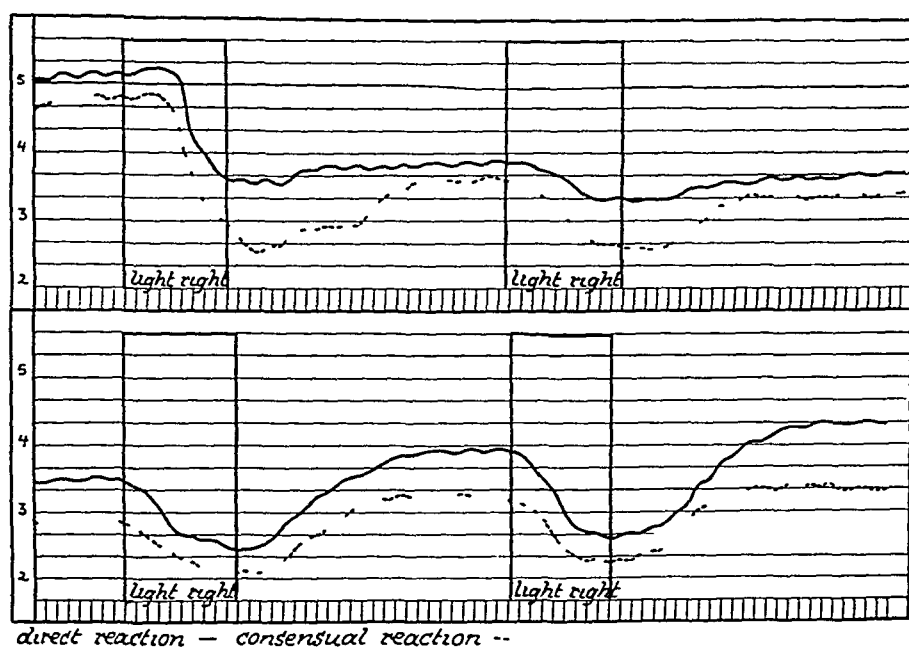


Fig 4—First line, “descending pupil”, second line, “climbing pupil”

We are able to state that the reflex to darkness is frequently more susceptible to the influence of pathologic conditions than is the reflex to light. We have found modifications of the reflex to darkness more frequently than of the reflex to light in cases in which neurologic lesions were known to exist. It is interesting to note that in man the secondary dilation phase is the portion of the reflex to darkness most prone to disappear (fig 5, *B 4*) when a pathologic condition is present, a fact which perhaps indicates that the phylogenetically youngest part is the most vulnerable one. Any of the abnormal patterns of the darkness reflex may coexist with either a perfectly normal reflex to light or a pathologic one. The deviations from normal in the light reflex may seem to be contrary to the abnormal features of the reflex to darkness or may be consistent with them. We may say, then,

3 Lowenstein, O., and Friedman, E. D. Adie's Syndrome (Pupillotonic Pseudotabes). *Arch Ophth* 28 1042 (Dec) 1942

that there is some independence of the two reflexes from one another, but, on the other hand, the same lesion may be able to destroy them both, in whole or in part

These dissociations of the two reflexes suggest that the reflex to darkness is more than a simple reversal of the reflex to light. Such a supposition as this is not an unusual concept to psychologists, who have emphasized the fact that a short interruption of a constant stimulus is effective as a new stimulus

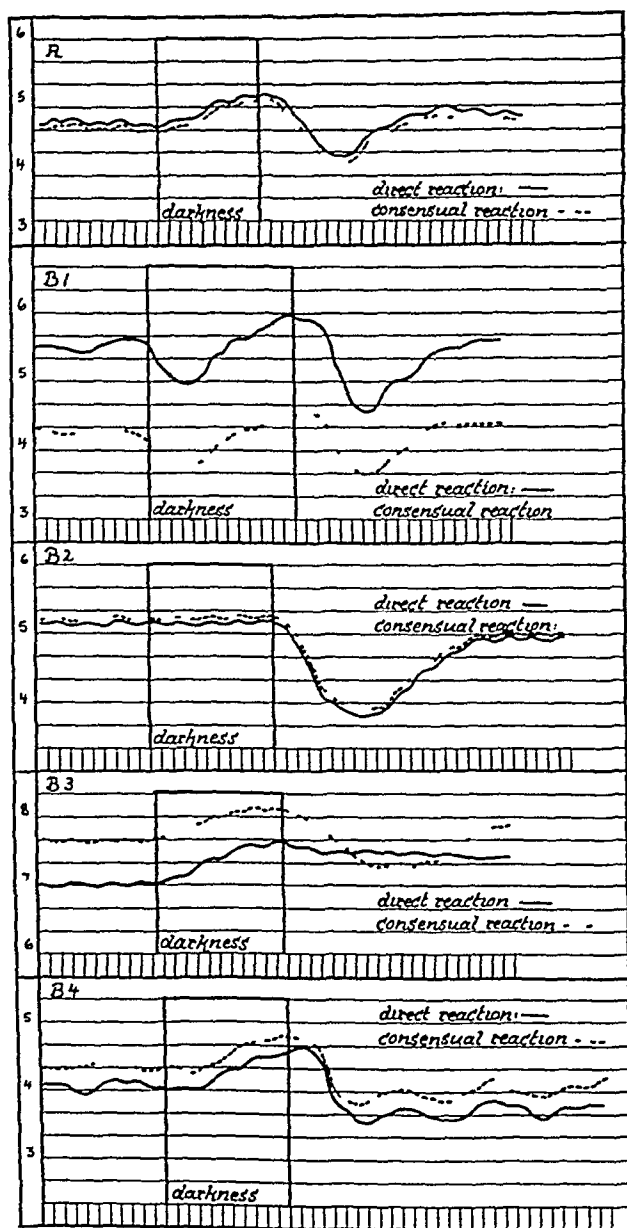


Fig 5—Pathologic variations of the reflex to darkness (*A* shows the normal reflex) *B1*, dilation preceded by a preliminary contraction, *B2*, primary dilation absent and the secondary phase normal, *B3*, the secondary phase absent in the directly stimulated pupil, *B4*, the secondary dilation phase absent (monkey type)

We are unable to say anything definite as to the anatomic basis of the dissociation. The types of pathologic disturbances and dissociations described point to the likelihood that both common and separate pathways are utilized in the reflexes to light and to darkness

We wish to report a case which may shed a little light on the problem of the nervous pathways through which the reflex to darkness travels

The patient, a youth aged 18, had been suffering from headaches and diplopia for approximately five months. He had had disturbances of his gait, mental dulness and vomiting for two or three weeks.

When examined on Jan 3, 1941, he showed 2 D of papilledema in each eye, a limitation of upward gaze and fixation of the pupils to light and convergence. Ventriculography confirmed the clinical diagnosis of tumor of the pineal body.

On January 5 he was operated on by Dr John B Scarff. The pineal body was exposed by an approach along the falx, and a total gross removal of a fairly firm, lobulated, well demarcated tumor was done. Postoperatively, there was a transient episode of psychotic behavior.

On April 5, 1942 it was found that clinically the pupils did not react to light but reacted to convergence promptly (Argyll Robertson phenomenon). Both optic disks showed temporal pallor. There was marked irregular concentric contraction of the visual fields of both eyes. The vision was 20/20 in both eyes.

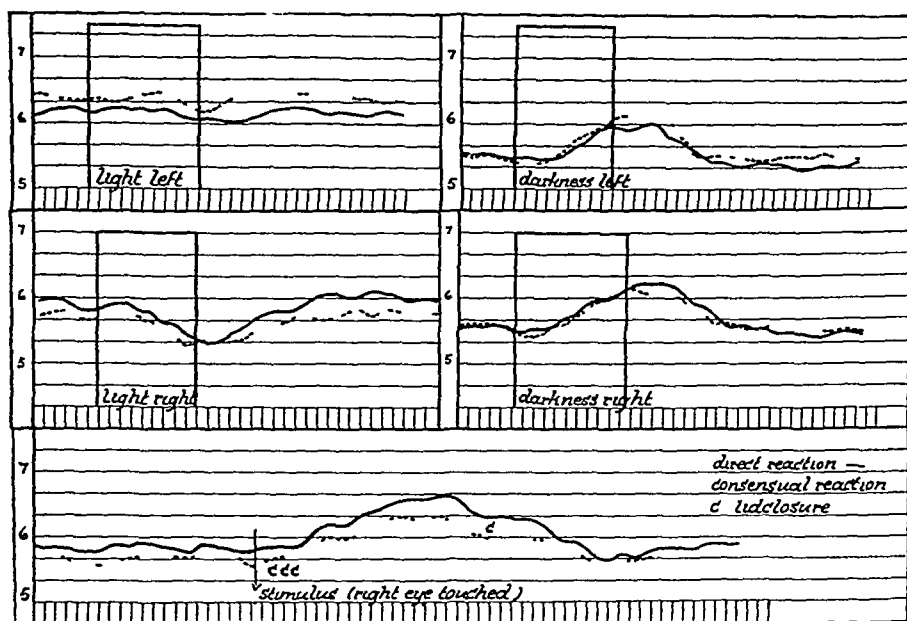


Fig 6—The pupillary reflexes in the case reported. The first line shows that the reflex to light is absent and the reflex to darkness present on the left side, the second line, that the reflex to light is diminished and the reflex to darkness exaggerated on the right side, and the third line, that the sensory dilation reflex is normal.

On July 7 the pupils still showed the same behavior. The fields of both eyes had improved. There was a paresis of the left superior rectus muscle. The pupil again showed an Argyll Robertson phenomenon. When the patient attempted to look upward and to the left his left eyeball underwent retraction and propulsion about four times (rotatory nystagmus). During this period the right eye displayed coarse and slow nystagmoid motions.

Pupillographic Studies—The reflex to light was absent on the left side and greatly diminished on the right side. The light reaction of the right pupil amounted to 0.66 mm. The consensual reaction of the left pupil, which did not react to direct stimulation by light, amounted to about 0.33 mm. The reaction to light of the right pupil was sluggish and had a latency period of about 0.5 second (normal, less than 0.3 second). It is striking that the second light stimulus and all subsequent ones in a series of repeated stimulations provoked reactions to light which were more rapid than the first one. Nevertheless, the reaction did not become more extensive than 0.5 mm on either side.

Stimulation by sound provoked a dilation on both sides of about 1.3 mm. The psychosensory restitution phenomenon was fairly effective on both sides after a sound stimulus, for example, both pupils reacted to light to an extent of about 0.66 mm and the latency period decreased to 0.4 second from its former level of 0.5 second.

The spontaneous lid closure reflex was absent. The pupillary reflex to conjunctival stimulation, however, was present and showed a fully developed dilatation. The reaction to near vision was present.

Primary dilation to darkness was present and about equal in the two eyes. It amounted to 1 mm or more (fig 6). The secondary phase of the reflex to darkness was present, but the secondary redilation phase was absent (a configuration found in the monkey).

We wished to know whether or not Argyll Robertson pupil (on a nonsyphilitic basis) is associated in all cases with an undiminished, or perhaps even an exaggerated, reflex to darkness. We therefore examined another patient, a 22 year old man with a tumor of the superior colliculus. He displayed a fully developed Argyll Robertson pupil, with paralysis of upward gaze. The reflex to darkness was absent.

CONCLUSION

In a patient operated on for pinealoma, we observed a dissociation between the reflexes to light and to darkness. The former were practically absent, and the latter were exaggerated.

This dissociation of pupillary reflexes suggests the existence of separate pathways for the reactions to light and to darkness. We cannot precisely localize the lesion in the pathways of the light reflex in the case reported, since no anatomic evidence is available.

We can state, however, that there must exist at least one point in the brain where the pathways of the reflexes to light and to darkness are not identical. This dissociation between the reflexes to light and darkness is not a universal characteristic of the nonsyphilitic Argyll Robertson phenomenon, since it was not demonstrable in a case of Argyll Robertson phenomenon due to a tumor of the superior colliculus.

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GENETIC STUDIES ON ECTOPIA LENTIS

A PEDIGREE OF SIMPLE ECTOPIA OF THE LENS

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The present report on the inheritance of ectopia lentis is based on the study of a single kindred displaying this relatively rare ocular anomaly. The pedigree includes six generations, the first two of which are known only from historical evidence supplied by the descendants. A total of 157 of the descendants were examined in their homes or in the University Hospital ophthalmic clinic, where slit lamp and refraction facilities were available. Twenty-four with ectopia lentis were observed, and the history of 5 other persons suggested probable dislocation of the lenses. In addition, 2 unaffected members were regarded as gene carriers, since they possessed affected children and grandchildren.

Besides the ocular examinations of members of the various families belonging to this kindred, several other tests and measurements were made, including anthropometric measurements, serologic tests of blood and saliva, determination of the taste reaction to phenylthiocarbamide, tests of color vision and eye dominance, tests of handedness and dermatoglyphic studies of the fingers, palms and soles. Blood samples were tested with respect to the blood groups (O, A₁, A₂, B), the MN blood types and the Rh factor of Landsteiner and Wiener¹. The "secretor factor" was determined on the saliva by means of human A and B serums and anti-O ox serum. Data on these hereditary characters are of interest primarily in regard to their genetic linkage and will be reported in a separate article. The present paper will be concerned chiefly with the ocular findings.

Ectopia lentis, a congenital subluxation of the crystalline lens, has been the subject of intensive study since it was first described by von Graefe² in 1854. This ocular anomaly is most frequently manifested as a bilateral symmetric displacement (subluxation) of the lens, but occasionally there may be great differences between the two eyes in the degree of displacement. Associated ocular defects have been reported which vary greatly in the type and mode of expression in different families. Axial and lenticular myopia, coloboma of the iris, coloboma of the iris and lens, corectopia, iridodonesis, ectopia pupillae, megalocornea, miosis, amblyopia, strabismus and persistent pupillary membrane have been most frequently reported. Ectopia lentis has also been observed as an associated anomaly in the syndrome described first by Marfan,³ in 1896, under the name of dolichostenomelia.

Dr Falls is Walter R. Parker Scholar in Ophthalmology, University of Michigan.

Records of all persons described in this report are on permanent file in the Heredity Clinic, University of Michigan.

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1 Landsteiner, K., and Wiener, A. S. *J. Exper. Med.* **74**: 309, 1941.

2 von Graefe, A. *Arch. f. Ophth.* **2**: 255, 1854.

3 Marfan, M. A. *Bull. et mem. Soc. med. d'hop. de Paris* **13**: 220, 1896.

This syndrome, now commonly termed arachnodactyly, is characterized by (1) elongation of the long bones (especially those of the hands and feet), (2) spinal curvature (scoliosis and kyphosis), (3) dolichocephalic skull, (4) underdeveloped musculature, (5) pes planus and hammer toes, (6) pigeon breast, (7) absence of subcutaneous fat and (8) infantilism. Achard,⁴ in 1902 called attention to the associated ocular anomalies and to the fact that 40 to 60 per cent of arachnodactylous persons manifested some pathologic ocular condition: ectopia lentis, iridodonesis, nystagmus, congenital miosis, strabismus and anomalies of the lids and lashes.

Ectopia lentis is inherited as a dominant character in the vast majority of published pedigrees. This is true of the simple forms as well as of those accompanied by ocular or other defects. Minor degrees of the defect are frequently overlooked unless careful ophthalmologic examination is made, and this may account for some of the familial cases. Complete failure of expression of the gene in certain heterozygotes or occasional mutation may account for other cases of a familial or sporadic nature. True recessive inheritance of this defect is probably rare since only 3 or 4 cases of parental consanguinity have been reported.

Judging from the genetics of other human and animal abnormalities, it is probable that several different mutations, at the same or at different chromosome loci, are responsible for the varying forms of hereditary ectopia lentis in different kindreds. The available data are too limited to permit of a precise analysis. It is our hope to make available more adequate data for the classification of this hereditary anomaly through a series of studies of several pedigrees.

A dominant gene is expected to be transmitted by an affected person to approximately 50 per cent of his or her offspring. In turn, an affected person is expected to have an affected parent. The normal siblings of involved persons will have children without the anomaly in question.

From the practical standpoint, the marked variability in the expression of some dominant genes is important, since the ophthalmologist is not always capable of distinguishing a person heterozygous for the abnormal gene. The oculist should attach a guarded prognosis to genetic advice given to afflicted persons and their offspring. It is known that unigenic ocular anomalies may adopt different hereditary patterns in different families. Thus there arises the necessity for individualization of all patients supported by intensive study of their peculiar pedigrees. Satisfactory but slow progress is being made by clinics of human heredity in the study of linkage of the standard test factors with abnormalities. It is believed that such study will provide more accurate detection of the absence or presence of the abnormal gene in a subject and thus permit of more scientific advice to prospective parents.

METHOD OF INVESTIGATION

The pedigree chart (fig 1) differs from the conventional diagram by having the children of a single union arranged vertically rather than horizontally. The sibships are numbered 1 to 58 and a particular person will be referred to by means of the sibship number followed by a number denoting his or her position (from top to bottom, corresponding to birth order) within the sibship. Thus, 18-3 and 18-4 are sisters, both with ectopia lentis, who married brothers, 20-4 and 20-8, thereby producing sibships 42 and 43, respectively. No information is available concerning the sibs of 1-1. The complete and exact order of birth of sibship 2 is open to question.

4 Achard, M. C. Bull. et mem. Soc. med. d. hôp. de Paris 19 834, 1902.

Our investigation started with affected sister and brother 32-3 and 32-4, who received the diagnosis of congenital dislocation of the lenses when examined at the ophthalmic clinic in 1935. This pair, therefore, must be regarded as the *propositi* of the kindred, and at the outset of the investigation no other members of the group were known. An interview with the parents and grandparents quickly established the dominant pattern of inheritance, and the defect was traced almost certainly to 1-1, who resided in Germany. Three children of this man immigrated to Ohio and left descendants, almost all of whom were known to reside in and about Toledo. It was then decided to examine all of these persons with care, and a complete pedigree was drafted before actual examination was undertaken. Subsequently it was discovered that 3 other members of the kindred had previously visited the University Hospital for ocular or other complaints. A complete

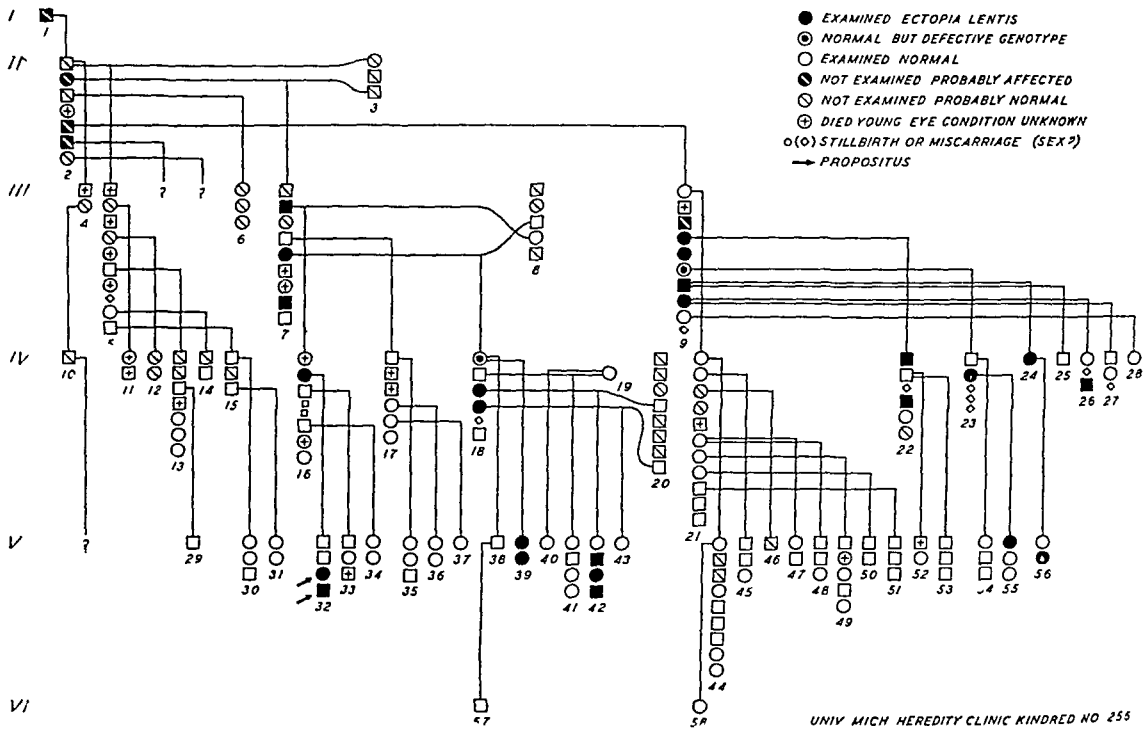


Fig 1—Pedigree chart

ophthalmologic examination was performed at the University Hospital ophthalmic clinic on the following members of the pedigree: 7-2, 9-5, 9-6, 9-8, 9-8b, 13-5, 13-6, 16-2, 18-1, 21-8, 21-8a, 23-2, 24-1, 26-1, 26-3, 27-1, 27-2, 32-1, 32-2, 32-3, 32-4, 34-1, 39-1, 39-2, 50-1, 50-2, 55-1 and 56-2.

Figure 1 shows all of the known descendants of 1-1. The spouses of these descendants were examined, and none were found to exhibit signs of ectopia lentis or related defects. None of the spouses are illustrated on the pedigree chart except in 1 instance in which the wife had a child (40-1) by an earlier marriage, and in 3 instances in which double family marriages occurred, producing three pairs of double first cousin sibships, 5 and 7, 16 and 18, and 42 and 43. The last 2 combinations were produced by sibs marrying sibs, both displaying ectopia lentis. This would not be expected to alter the probability of defective children, though it might account for an increased similarity in degree of manifestation of the defect in these cousins if some of the variability in this respect was attributable to modifying genetic factors.

Genealogic information concerning the spouses was not secured except in certain cases in which we became interested in other genetic characters, such as color blindness and twinning. It is not definitely known, therefore, whether most of the unions were free from consanguinity. Where it was necessary to refer to some of the spouses this was done by attaching a letter *a* or *b* to the number of the descendant in question. Thus, 5-10*a* was the wife (not shown) of 5-10, while 9-8*b* was the second husband of 9-8 and the father of sib 27.

OCULAR ANOMALIES OF THE AFFECTED MEMBERS

Figure 2 represents the pathologic changes observed in the affected members of the kindred with the ophthalmoscope and the slit lamp when used. The pupils were not dilated in the majority of cases, and the drawings represent the lenses as seen

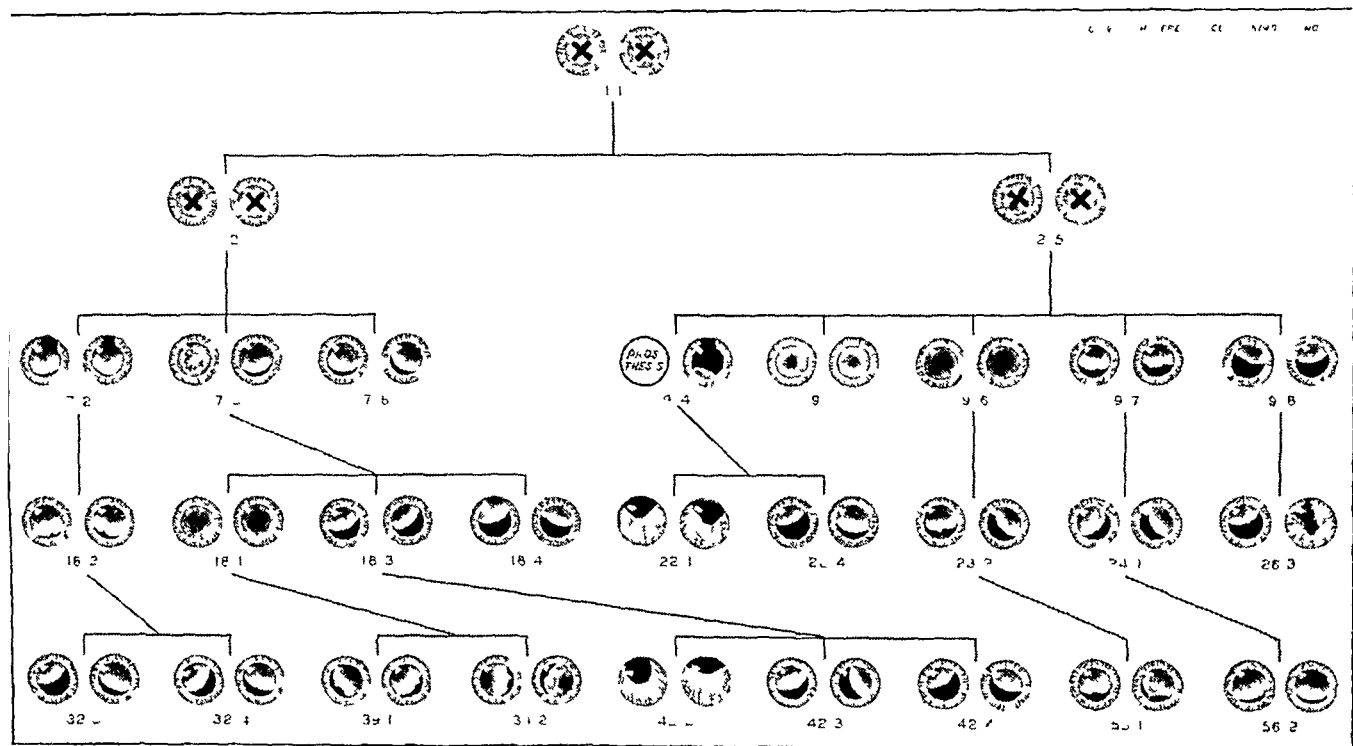


Fig 2—Pathologic changes observed with the ophthalmoscope and the slit lamp in the affected members of the kindred

through the undilated pupils. A brief description of the pathologic changes and ocular anomalies for each subject follows.

1-1 This man constituted the probable ultimate source of the hereditary defect in the kindred. He resided in Germany near the city of Stolp, in Hinterpommern. Information regarding him was obtained chiefly through his grandson 7-2, as follows: "One day, after working many hours in the field in the hot sun, my grandfather plunged his face into a bucket of cold water, and shortly afterward severe pain in his eye developed. The eye became blind, but I do not know which one. This happened when he was between 40 and 50 years of age." We interpret this episode to indicate probable secondary glaucoma resulting from displacement of the lens into the anterior chamber in view of the similar experiences of his descendants. The wife of this man was described as having normal eyes. Four of his children, 2-1, 2-2, 2-3 and 2-5, immigrated to Lucas County, Ohio, but 2-3 returned to Germany with his 3 daughters and no further information concerning his descendants was available.

2-2 This woman was known always to have had poor visual acuity and had had numerous episodes of severe ocular and head pain. The vision of one eye was lost after a severe bout of such pain. We again interpret these symptoms as sequelae of dislocated lenses.

2-5 This man was always near sighted. Episodes suggesting secondary glaucoma in the right eye were experienced at the age of 70 and again at 78, at which time this eye

was removed. We were informed by Dr R E Boice of Toledo, Ohio, that the left eye showed a dislocated lens at the age of 80 and that the patient was under medical treatment for glaucoma. Although he was described as being 6 feet 1 inch (185 cm) tall, with a maximum weight of 135 pounds (61 Kg), signs of arachnodactyly were not evident in photographs or in descriptions by his children. Unfortunately this study was not initiated until six months after the man's death, at the age of 86, in January 1942.

7-2 At the age of 60 this man submitted to surgical treatment for the relief of chronic noninflammatory glaucoma. Bilateral iridencleisis was performed, with excellent subsequent control of the intraocular tension. At the age of 67 observation revealed that in each eye the lens was dislocated minimally up and out, was maturely cataractous and displayed a minute notch, or coloboma, inferiorly. Fundusoscopic examination disclosed glaucomatous optic nerve atrophy in each eye. The right eye was blind, and the visual acuity in the left eye uncorrected was 3/60 and with correction was 6/30. The tension (new Schiøtz tonometer) was 12 mm in each eye. There was 8 to 10 degrees of left divergent strabismus (Priestley-Smith).

7-5 This 60 year old woman stated that she had had cataracts as a child and that vision in the right eye was lost after an episode of severe ocular pain. On examination the right eye was found to be blind and the visual acuity of the left 1/60 uncorrected. There were marked ectasia and dense scarring of the cornea in the right eye. The right lens was irregular, shrunk, partially calcified and held in place by dense synechias. Finger tension was 4 plus in the right and normal in the left eye. The left lens was maturely cataractous and dislocated up and in, as shown in the diagram. The left fundus was normal except for mild arteriosclerosis of the retinal vessels. Fifteen degrees of right divergent strabismus was demonstrated (Hirschberg).

7-8 This 59 year old asthenic man, a farmer, had married late in life and was without issue. His eyes were straight. There was marked iridodonesis, especially of the lower half. Both lenses were dislocated up and slightly out, with an irregular, slightly notched lower border. The visual acuity was 6/9 — 1 in the right and 6/21 — 1 in the left eye uncorrected. No fundus disease was observed.

9-3 This man had died without issue and was described by his brothers and sisters as having had "bad eyes." No definite details could be obtained, but he was regarded on the pedigree chart as "probably affected."

9-4 This 54 year old woman had had the right eye enucleated at the age of 28, it had been blind and painful, with anterior dislocation of the lens. At the age of 47 a complete iridectomy of the left eye was performed for relief of chronic noninflammatory glaucoma. This eye displayed a large complete surgical coloboma of the iris at 12 o'clock. Conspicuous iridodonesis was observed. The lens was completely cataractous and had gravitated into the vitreous below.

9-5 This 52 year old woman had married late in life and was without issue. Her uncorrected visual acuity was 6/15 in the right eye and 6/30 in the left eye. An incipient alternating divergent strabismus of 8 to 10 degrees was present. The irises were a light gray-blue. No iridodonesis was demonstrable. Slit lamp examination revealed long attenuated zonular fibers conspicuously especially from 5 to 8 o'clock in the right and from 3 to 7 o'clock in the left eye. An occasional ruptured zonal fiber could be seen freely waving in the aqueous. Minimal, but conspicuous, lenticular nuclear sclerosis was present in both eyes. The fundusoscopic examination gave normal results except to show minimal arteriosclerosis of the retinal vessels and minor macular degenerative changes in both eyes. The visual fields were normal for both eyes. The patient accepted the following manifest correction:

Right eye	+ 0.75 D sph	⊂	+ 0.25 D cyl, axis 98,	vision, 6/45 — 4
Left eye	+ 1.25 D sph	⊂	+ 0.37 D cyl, axis 57,	vision, 6/45 — 5
Both eyes	+ 2.25 D sph for reading, for Jaeger type 1 at 31 cm			

9-6 This 50 year old woman had no ocular complaints other than those of presbyopic origin. The uncorrected visual acuity was 6/12 — 2 in the right and 6/12 in the left eye. The external examination gave negative results except to show incipient alternating divergent strabismus. Fundusoscopic examination revealed spicules of incipient senile cataract in the inferior nasal quadrant of each lens. Moderate arteriosclerosis of the retinal vessels without retinopathy was present in both eyes. No iridodonesis was demonstrable, and meticulous slit lamp examination failed to reveal any signs of pathologic change in the lenses or zonules. Gonioscopic examination did not reveal any anomaly of the anterior chamber angles.

9-7 This 47 year old asthenic man, a farmer, exhibited 5 degrees of left divergent strabismus (Priestley-Smith). There was conspicuous iridodonesis in each eye. Both lenses were dislocated up and out, the left more markedly. A conspicuous coloboma was present in

the lower border of each lens. The vision was 6/9 —2 in the right and 6/60 in the left eye uncorrected. The fundi were normal.

9-8 This 40 year old woman exhibited 15 degrees of right divergent strabismus (Priestley-Smith). Both lenses were dislocated up and out and were immaturely cataractous. Marked iridodonesis was present in both eyes. The vision was 5/60 in the left eye uncorrected and 6/9 —2 in both eyes with correction.

16-2 This 39 year old woman gave a history of episodes of blurred vision accompanied by haloes about lights. The intraocular tension was 26 mm of mercury in each eye with the pupil undilated and 12 mm with the pupil dilated (new Schiøtz tonometer). The corrected visual acuity was 6/60 in the right and 6/6 —2 in the left eye with a minor correction for compound myopic astigmatism. Prominent iridodonesis was present in both eyes. Both lenses were dislocated up and out, and each presented a small coloboma in the inferior border. The fundusoscopic examination revealed nothing abnormal except hypertensive retinitis in each eye, grade III (Keith-Wagener).

18-1 This 41 year old woman had visual acuity of 6/6 —3 in the right and 6/9 —4 in the left eye without correction and of 6/6 and 6/6 —1 with correction. External ocular examination revealed only a few degrees of alternating divergent strabismus. The point of basal convergence was 130 mm. There was no evidence of iridodonesis or other indication of ectopia lentis. The fundi were normal except for grade III (Keith-Wagener) hypertensive retinitis without retinopathy. A minor compound hyperopic correction was worn.

18-3 This 34 year old woman had submitted to extraction of a completely dislocated lens in the right eye and secured a satisfactory result. The vision in both eyes was 15/60 without correction and 6/9 —3 with correction. Iridodonesis was present in both eyes. There was a complete surgical coloboma of the right iris with incarceration of the temporal pillar. The left lens presented zonular cataractous changes and was dislocated up and out to a degree sufficient to give aphakic vision. No gross fundusoscopic change was observed except peripheral inactive chorioretinitis in the left eye.

22-1 This 30 year old mechanic had experienced dislocation of the right lens into the anterior chamber in September 1940. The lens was successfully extracted by Dr J L Roberts, of Toledo, Ohio. The left lens became dislocated into the anterior chamber two months later, and the same surgeon secured a similar good result. The vision was 15/60 in both eyes uncorrected and 6/9 +3 in the right and 6/9 —2 in the left with correction. Examination of the fundi disclosed many opacities of the vitreous but no retinal disease. A complete surgical coloboma of the iris was present superiorly, and both pupils were boat shaped.

22-4 This 22 year old man was not willing to submit to examination by us, but details were obtained from his local ophthalmologist. His vision in 1931 was 6/60 in the right and 6/30 in the left eye uncorrected and with correction 6/30 +2 and 6/30. The lenses showed no cataractous changes but were dislocated up and out. No retinal disease had been observed at that time.

23-2 This 27 year old asthenic woman, a housewife, manifested 10 degrees of left divergent strabismus (Priestley-Smith). Her uncorrected vision was 6/21 in the right and 1/60 in the left eye. The external examination disclosed mild paresis of the right inferior oblique muscle. Complete iridodonesis was evident in both eyes. The lenses were dislocated up and out. No important fundusoscopic changes were present.

24-1 This 27 year old asthenic woman had uncorrected visual acuity of 6/21 in the right and 1/60 in the left eye. There was 15 degrees of left divergent strabismus. There was iridodonesis in each eye, and both lenses were dislocated up and out. Both disks were best seen with a —20 lens. A small inferior myopic temporal conus was visualized in each eye. The lower border of the right lens was deeply notched, as illustrated. The central inferior portion of the lens was pulled out into a tag by adherent zonular fibers. The picture was similar but less pronounced in the left eye.

26-3 This 19 year old youth experienced dislocation of the left lens into the anterior chamber in 1934, and extraction was attempted. Considerable vitreous was lost during the surgical procedure, with subsequent organization of the vitreous and retinal detachment. Examination revealed 10 degrees of left convergent strabismus. Paresis of the external rectus muscles was demonstrated. Iridodonesis was present in both eyes. The finger tension was subnormal in the left eye. The left cornea was scarred and exhibited band keratitis. There was a complete surgical coloboma above. The pupillary opening was filled with a dense gray membrane. No fundus details were visualized in the left eye. The right lens was dislocated up and out, the lower border of the lens crossing in the middle of the pupillary opening. No fundus disease was seen in the right eye. The slit lamp examination revealed minimal notching in the lower border of the lens, and fluid vitreous could be seen bulging into the

anterior chamber The visual acuity was 6/30 in the right eye with a correction of + 12.50 D sph \ominus + 1.75 D cyl, axis 168

32-3 This asthenic 17 year old girl had uncorrected vision of 2/60 in both eyes With correction the vision was 6/9 — 2 in the right and 6/12 — 3 in the left eye There was definite iridodonesis in both eyes Both lenses were dislocated up and out, the right more markedly The fundi were normal The refractive error through the phakic portion of the pupil was

Right eye — 8.00 D sph \ominus — 6.00 D cyl, axis 115 vision, 3/60
Left eye — 8.00 D sph \ominus — 10.00 D cyl, axis 70, vision, 2 5/10

Through the aphakic portion of the pupil the error was

Right eye + 11.00 D sph \ominus + 2.00 D cyl, axis 112, vision, 6/9 — 2
Left eye + 10.50 D sph \ominus + 2.50 D cyl, axis 65, vision, 6/12 — 3
Both eyes + 2.50 D sph for reading, Jaeger type 4, right eye, and
Jaeger type 1 at 26 cm, left eye

32-4 This asthenic 16 year old boy had uncorrected visual acuity of 1/60 in both eyes External ocular examination gave negative results except to reveal iridodonesis in both eyes Both lenses were dislocated up and out to a degree which permitted aphakic vision The fundi were normal The refractive error through the aphakic portion of the pupil was

Right eye + 13.00 D sph \ominus + 0.75 D cyl, axis 115, vision, 6/9 — 1
Left eye + 13.00 D sph \ominus + 0.75 D cyl, axis 72, vision, 6/9 — 1
Both eyes + 2.50 D sph for reading, Jaeger type 1 at 26 cm

39-1 This stocky 16 year old girl had uncorrected vision of 6/12 — 2 in the right and 6/9 — 3 in the left eye There was iridodonesis in both eyes Both lenses were dislocated up and in The fundi were normal

39-2 This slim 14 year old girl had uncorrected visual acuity of 6/12 — 3 in both eyes The eyes were straight at times, and at other times there was a few degrees of alternating divergent strabismus Mild paresis of the superior rectus muscles was demonstrated There was iridodonesis in both eyes Both lenses were dislocated down and out, with notching as illustrated The fundi were normal except for astigmatic distortion

42-2 This asthenic 13 year old boy was aphakic in both eyes, having submitted to surgical intervention for dislocated lenses three years before our examination There was 8 to 10 degrees of left divergent strabismus The left pupil was large and boat shaped, as illustrated Incarceration of the iris pillars was present in both eyes There was conspicuous iridodonesis in both eyes The fundi showed marked myopic temporal conus and myopic retinal degeneration The visual acuity was 1 5/60 in both eyes uncorrected and 6/15 — 2 in the right and 6/60 in the left corrected

42-3 This 7 year old girl had uncorrected visual acuity of 3/60 in both eyes The eyes were straight in the primary position, but there was paresis of the superior rectus muscles Iridodonesis was present in both eyes The lenses were dislocated up and out, the left more laterally Posterior subcapsular opacification was noted in both eyes Mild myopic changes in the retina were seen in both eyes

42-4 This stocky 4 year old boy would not cooperate sufficiently to permit an adequate impression to be gained of his visual acuity Most of his ocular habits indicated a rather high myopic error of refraction The eyes were straight, but there was paresis of both inferior oblique muscles Iridodonesis was present in both eyes Both lenses were dislocated up and out No fundus details could be seen because of the poor cooperation, however, no cataractous changes were observed in either eye

55-1 This stocky 6 year old girl had uncorrected visual acuity of 6/20 — 1 in the right and 3/60 in the left eye The eyes were straight at times and showed a few degrees of alternating divergent strabismus at others There was paresis of the right superior rectus muscle There was iridodonesis in both eyes The left pupil was 1 mm larger than the right Both lenses were dislocated up and out The fundi were normal

56-2 This stocky 3 year old girl could not be tested for visual acuity, but gross tests with objects indicated reduced vision in both eyes An incipient alternating divergent strabismus was present The lenses were dislocated up and out An associated iridodonesis was seen in both eyes A minute coloboma of the inferior border of each lens could be seen The fundus examination gave negative results

The ectopia lentis as expressed in this pedigree is obviously produced by a dominant gene A most interesting variability of expression is present, the degree

of lenticular dislocation running the gauntlet from gross normality to complete luxation. Two women, 18-1 and 9-6, at their present ages of 40 and 50 show no gross anomaly of the lens zonules or position. Though apparently normal, these women must certainly possess the morbid gene, since they are children of defective parents and in turn have produced defective children and grandchildren. The woman 9-5 would have been considered normal if slit lamp examination had not been performed. The theory of "lack of penetrance" of the abnormal gene affords a rather unsatisfactory genetic explanation for such variability of expression. Also, it is not known whether the gene is fully dominant to the normal allele, since homozygotes for the defective gene are not known and in the heterozygous condition there is such a variable expression of the character. It would perhaps be better to call the abnormal gene a nonrecessive. True recessive inheritance of this defect is probably very rare, since, as previously stated, only 3 or 4 cases of parental consanguinity have been reported.

OTHER ABNORMALITIES

Strabismus—One hundred and nineteen persons were examined for gross evidence of strabismus. Among the 25 exhibiting ectopia lentis, 15, or 60 per cent, displayed some variety of strabismus, 9 had eyes which were straight in the primary position, and 1 had monocular prosthesis. Only 5, or 5.3 per cent, of the persons without ectopia lentis evidenced any gross strabismus.

Myopia—Except in 24-1, 42-2 and 42-3, the myopia observed in the affected members was of lenticular, rather than axial, origin. Aphakic errors of refraction, such as +13.00 to +15.00 D sph, and the absence of myopic retinal degenerative changes support this finding. It has been our experience that most of the myopia is of lenticular origin in kindreds showing ectopia lentis. Indeed, it has been so frequently observed that we have come to regard compound myopic astigmatism as one of the minor criteria by which the diagnosis of ectopia lentis can be supported when other signs are not too clear.

Corneal Horizontal Diameter—The corneal horizontal diameter was measured in all members of this kindred and ranged from 10.0 to 12.1 mm. This is well within the range of normal variation, and there has been no association of the ectopia lentis with microcornea or megalocornea in this group.

Lenticular Coloboma—Coloboma of the lens was noted in 16-2, 23-2, 9-7, 39-2, 39-1 and 55-1. In the last 2 the defect was not apparent on gross examination but was revealed with the slit lamp. It is probable that some other affected members would have shown this anomaly had they been subjected to slit lamp examination. It was interesting to note that the coloboma resulted in areas in which the zonular fibers were absent or broken off, the indentation of the lens being apparently produced by the fibers' elastic recoil.

Iris—We were unable to diagnose a single case of congenital corectopia or coloboma of the iris in this kindred. The observation of the color of the iris led to the conclusion that iris pigmentation is governed by factors independent of that producing ectopia of the lens. A slight pallor of the iris or heterochromia was noted in most eyes showing ectopia of the lens. This may have been the effect of mechanical trauma to the pars retinae iridis or an actual developmental anomaly of the "iris pigment."

Miosis—Nothing conclusive can be said concerning incomplete development of the dilator fibers of the iris in this kindred, as mydriatic drugs were employed in too few cases. The affected and nonaffected members who underwent refraction

under cycloplegia did not display any inability of the iris to dilate. No abnormality of pupillary reflex action to direct light, consensual light or accommodation was noted in any member of the family examined. Serologic tests of the blood of all members examined at the University Hospital gave negative results.

Persistent Pupillary Membranes—Persistent pupillary remnants or membranes were a frequent finding, but they occurred with approximately equal frequency in those persons having, and in those lacking, ectopia of the lens. Approximately 20.3 per cent of the eyes examined had minor degrees of this abnormality of the iris.

Anthropometric Measurements—None of the affected members of this kindred showed skeletal deformities of a degree sufficient to permit the diagnosis of Marfan's syndrome. Nevertheless, the possibility that the abnormality might be accompanied by less pronounced changes in the long bones prompted the inclusion of 6 anthropometric measurements in the examinations. These comprised (1) total stature, (2) span, (3) biacromial measurement, (4) length of the left hand, (5) width of the left hand and (6) length of the left middle finger. All members of the kindred were measured except the younger children. Statistical analysis of the data failed to reveal an association between any of these measurements and the defect of the lens. After adjustment for age variations, the variance between affected and unaffected like-sexed sibs was in no case significantly greater than the variance among sibs of like sex and ocular conditions. There is no suggestion so far as these measurements are concerned that ectopia lentis is related to the genetic syndrome of arachnodactyly.

Gonioscopic Findings—Gonioscopic examination was performed on 7 of the affected members. No abnormality of the filtration angle was noted with the exception of gross irregularity in its depth. This had been anticipated in view of the lenticular dislocation and tilting. Subject 7-2 presented a narrow angle glaucoma type of filtration angle with numerous peripheral anterior synechias. His iridocyclitis opening was satisfactory in each eye.

Cataracts—In this pedigree a comparison of the nonaffected and affected persons of the same age as to the presence of cataractous changes indicates that the dislocated lens is predisposed to opacification. It is probable that the interference in the normal physiology of the dislocated lens may also result in metabolic disturbances which terminate in cataractous formation.

Glaucoma—In this study glaucoma, either secondary to complete luxation of the lens in the anterior chamber or primary noncongestive, was a frequent sequela of ectopia lentis. Anterior chamber luxation is thought or is known to have occurred in 1-1, 2-2, 2-5, 7-5, 9-4, 18-3, 22-1, 22-3 and 42-2. Primary noncongestive glaucoma had been diagnosed and surgically controlled in 7-2. Glaucomatous symptoms had been experienced by 16-2 and 18-2. No member of the pedigree who was normal so far as ectopia lentis is concerned displayed any evidence of glaucoma despite a constant search for the disease. All affected members of this pedigree were warned of the possibility of glaucoma occurring and of its serious sequelae.

TREATMENT

The treatment of ectopia lentis is preferably prophylactic. All affected persons should be made acquainted with the genetic pattern of inheritance of the anomaly and impressed with the consequences of having children. All offspring of affected persons should be subjected to a most complete ocular examination by a competent ophthalmologist in order to rule in or out the presence of ectopia lentis. When the anomaly is found, refraction with or without cycloplegia should be attempted to

secure the most satisfactory visual acuity through either the phakic or the aphakic portion of the pupillary opening. Refractive correction should be prescribed as early in life as possible in an attempt to prevent the development of amblyopia and accommodative divergent strabismus.

Ectopia lentis is not often a surgical problem unless the visual acuity is extremely poor or luxation of the lens into the anterior chamber occurs. The latter complication occurs most frequently shortly after the patient retires, when the room is dark and he is in a supine position. We have routinely suggested that physostigmine salicylate ointment (0.25 per cent) be instilled into the conjunctival cul-de-sac when the patient retires in an attempt to prevent this serious complication.

The patient with ectopia lentis with the lens in the anterior chamber presents a most serious surgical problem. Miotics are employed intensively in an attempt to constrict the pupil behind the lens preliminary to extraction. The patient is kept in a supine position on a Bradford frame during the administration of the miotic. When satisfactory miosis is secured the patient is placed prone on the usual cataract stretcher, and a corneoscleral suture is inserted. The lens is then fixated with a knife needle, and while the assistant steadies this the surgeon makes a scratch incision with a keratome or a von Graefe knife, since the anterior chamber is too shallow to permit the making of a regular corneal incision. After very slow decompression of the anterior chamber the incision is enlarged with Stevens' scissors. No iridectomy is performed. The lens is delivered with either a lens loop or an intracapsular forceps, according to which will prove more efficacious.

When the visual acuity is so poor that surgical intervention is indicated a great deal of individualization must be practiced. The position, character and extent of the lenticular displacement will determine the surgical approach. Optical iridectomy frequently gives a clear and sufficient opening for aphakic vision. In the case of nasal and inferior displacement of the lens, a carefully placed naso-inferior iridectomy may permit utilization of phakic vision. Discussion of a partially dislocated lens results in a high percentage of undesirable sequelae. A discussion with two knife needles followed by linear extraction when needed is suggested. The knife needles are inserted into the cornea at opposite meridians, one to fix and hold the lens and the other to rend the capsule and cortex. It is to be emphasized, however, that discussion performed in this manner requires considerable experience and is not an easy procedure.

Intracapsular extraction is fraught with danger, as a large number of the eyes present fluid vitreous. Removal of the lens by loop extraction is practically always followed by serious loss of vitreous.

Glaucoma is a frequent complication of ectopia lentis. The treatment of this must also be individualized. It is our policy to treat the eye as aphakic, and, of course, the operative procedure of choice is cyclodialysis.

To summarize, surgical intervention in the treatment of ectopia lentis is a serious and dangerous undertaking.

ECONOMIC CONSIDERATIONS

Visiting the homes of the various families gave us an unusual opportunity to witness the influence of ectopia lentis on the economic status, mental and physical well-being and range of education of the affected members.

Generally speaking, the level of intelligence was average in this kindred, with no exceptional variations noted in any sibship. The homes of most were moderate to poor, being characteristic of the lower income brackets. On the whole, the kindred was composed of pleasant personalities who enjoyed pleasing marital

congeniality The homes of the affected persons were distinctly inferior to those of their normal sibs with the exception of the farmers It was apparent that affected persons were limited in their choice of spouses

No exceptional educational achievement was evidenced by any of the kindred and most of the affected members had left school early because of their ocular handicap The lack of education was reflected in the type of vocation followed by the members with ectopia lentis

The mental and physical well-being is greatly influenced by the presence of ectopia lentis The affected person is impressed early in life with the fact that he is in some manner "different" from his playmates Childhood indifference and frankness emphasize this variation The lowered visual acuity limits the child in competitive sports and activities Competition in the present school system is great, and a prerequisite to success is good visual acuity, which, of course, the majority of the affected persons do not possess Thus, the child gradually falls behind his acquaintances and loses interest and self confidence, and he leaves school at the first opportunity Ocular pain and headache are the most frequent complications and possibly accompany episodes of increased intraocular pressure The pain described by some persons was so excruciating as to incapacitate them The ever present threat of dislocation of the anterior chamber with subsequent glaucoma was known to most of the affected members, who limited vigorous activity in accordance

A kindred of this character frequently becomes a burden to county and welfare funds This family is no exception Members 18-3 and 18-4 once were wards of the Toledo School for the Blind, 42-2, 42-3 and 42-4 had frequently been the recipients of county medical attention, 42-2 had two surgical interventions and, of course, had to be hospitalized, 24-1 and 23-2 also received county medical attention for their visual anomaly

Many of the affected members, both in financial and in personal care, had been a great burden to their parents and relatives, 32-3, 32-4, 7-2, 9-4 and 22-1 had all been frequent visitors to ophthalmic clinics and ophthalmologists, at no mean expense to their supporters, 7-2 was largely dependent on his wife and daughter for his support, 26-3, with one eye useless and the other amblyopic, was an economic liability to his parents, 7-8 and 9-7 were successful farmers, possibly because farming does not place such a premium on good visual acuity

SUMMARY

A pedigree of ectopia lentis is presented which displays dominant inheritance of the anomaly, with 2 instances of "lack of penetrance" of the abnormal gene

No conspicuous associated anomalies of the iris, cornea or pupil were observed Cataractous changes are common sequelae of the dislocation of the lenses

Chronic noninflammatory glaucoma and secondary glaucoma are frequently observed, and both carry a serious prognosis for preservation of the visual acuity

Anthropometric measurements taken on all members of this kindred failed to indicate any association between ectopia lentis and the length of the extremities such as is found in the syndrome of arachnodactyly

Ectopia lentis to a considerable degree adversely affects the physical and mental well-being, the educational achievement and the economic status of the affected person

Eugenic advice is of importance to both the unaffected and the affected members of a kindred exhibiting this dominant pathologic inheritance

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ELECTROPHORETIC STUDIES ON SERUMS OF PATIENTS WITH OCULAR DISTURBANCES

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AND

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CHICAGO

The electrophoretic technic of Tiselius¹ has been used by a number of workers to study the proteins in normal and in pathologic human serums.² In this method, a boundary is formed in a specially designed U tube between a solution of proteins in a buffer and an ultrafiltrate of the solution. The application of a potential gradient across the boundary causes the original single boundary to separate into a series of boundaries corresponding to the number of electrophoretically discrete protein fractions present in the original mixture (certain anomalous boundaries being excluded). The boundaries move toward the electrode of the sign opposite the charge on the proteins forming the boundaries. By use of a lens system developed by Philpot,³ and later modified by Svensson,⁴ the positions of the boundaries can be visualized and the concentrations of the protein components determined. In short, the components of a mixture of proteins are separated by their difference in mobility and the number and concentrations of the components determined.

The results obtained by Tiselius⁵ on horse serum, as modified by the later work of Longsworth and MacInnes,⁶ indicated that there are four components. Stenhagen,⁷ extending the work to human serums, found the same number of electrophoretically discrete fractions. The component occurring in the greatest concentration in the serum and possessing the greatest mobility has been shown to be albumin. The three remaining fractions are globulins and have been termed alpha, beta and gamma globulins. Moore and Lynn^{2c} made a statistical analysis of the concentrations of the various components of the protein of normal serums. Their results show that the concentrations of the four components are remarkably constant.

Longsworth, Shedlovsky and MacInnes,^{2b} in a study of the serums of 10 patients with various pathologic conditions, found notable changes in the electrophoretic components. Gutman and his co-workers^{2d} reported on extensive studies

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3 Philpot, J St L. *Nature*, London **141** 283, 1938

4 Svensson, H. *Kolloid-Ztschr* **87** 181, 1939

5 Tiselius, A. *Biochem J* **31** 1464, 1937

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made on the serums of patients with myeloma Seibert⁸ described changes occurring in the serum protein in association with tuberculosis

The investigations of Tiselius⁵ on horse serum, of Newell and co-workers⁹ on allergic human serums and of van der Scheer, Wyckoff and Clarke¹⁰ on anti-bacterial serums indicate that a great number of antibodies are associated with the gamma globulin fraction or with a fraction (T) with a mobility between that of the beta and that of the gamma fraction

The investigation of the serum proteins of patients with various ocular conditions was undertaken to determine whether the local pathologic process in the eye has a widespread effect on the body fluids The involvement of the uveal pigment and the lens, which have been shown to be antigenic¹¹ in various ocular disturbances, suggested that sensitization might occur and result in changes in the serum protein

Studies of serum proteins in cases of glaucoma by earlier methods¹² failed to disclose abnormalities However, the work of Cohn and his co-workers¹³ and Gutman and his group^{2d} on the comparative merits of salting-out technics and electrophoretic separation showed that the chemical method used in the earlier work is largely inadequate for determination of changes in the various fractions of the serum protein

METHOD

Blood was drawn into a test tube, and after it had clotted the serum was poured off and centrifuged The serum was diluted with 3 volumes of a buffer solution consisting of 0.025 molar lithium diethylbarbiturate, 0.025 molar diethylbarbituric acid and 0.025 molar lithium chloride, described by Longsworth, Shedlovsky and MacInnes^{2b} The buffer has a p_H of about 7.8 at 25 C The p_H , which was determined for each specimen with the glass electrode, was 7.8 ± 0.1 for all serums The diluted serum was dialyzed against 2 liters of buffer for at least forty-eight hours in the ice box, with merthiolate as a preservative After being filtered, the dialyzed serum was placed in the electrophoresis cell in the usual manner and the separation carried out Photographs of diagrams of the boundaries obtained with the Philpot-Svensson lens system were made, and the descending pattern was enlarged for determination of the areas under the peaks The concentrations of the various fractions were obtained from the descending areas The total protein concentration of the serum was determined by the falling drop method

RESULTS

The data obtained in the electrophoretic analyses of the serums of 18 patients with various pathologic ocular conditions are presented in the table For comparison, the statistical values of Moore and Lynn^{2c} for normal serums are also given Results of analyses of normal serums in the laboratory with which we are associated are in complete agreement with these values

^{6c} Before the changes in concentration of the serum protein fractions are considered, it must be pointed out that the patients used in this study for the most part had other pathologic conditions associated with the ocular lesions, these complicating states might be responsible for the changes observed or might mask

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Data Obtained in Electrophoretic Analyses of the Serum of the Eighteen Patients with Ocular Diseases

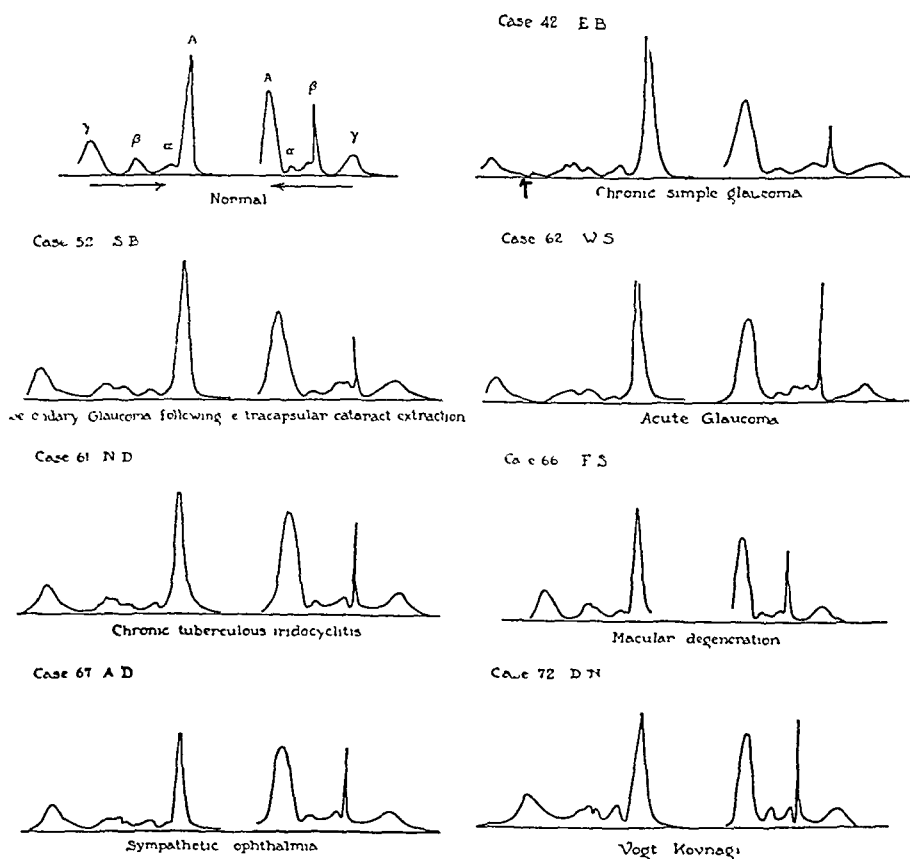
Patient	Case No	Ocular Condition	✓ Albumin		α-Globulin		β-Globulin		γ-Globulin		Total Protein*	Albumin*	Globulin*	X	α Fraction*	β Fraction*	γ Fraction*
			Albumin	Globulin	Albumin	Globulin	Albumin	Globulin	Albumin	Globulin							
J G	39	Chronic simple glaucoma	1.42		0.10	0.33	0.28		0.65		3.90	2.75	0.37	1.29	1.09		
W L	40	Chronic simple glaucoma	1.23		0.19	0.26	0.36		6.05		3.34	2.71	0.64	0.87	1.21		
E B	42	Chronic simple glaucoma	1.43		0.13	0.36	0.21		6.47		3.88	2.59	0.51	0.81	1.41		
E N	43	Chronic simple glaucoma	1.41		0.12	0.35	0.24		5.92		3.46	2.46	0.37	1.24	0.83		
R B	45	Chronic simple glaucoma	1.23		0.15	0.30	0.33		5.81		3.23	2.53	0.49	0.97	1.08		
W B	76	Chronic simple glaucoma	1.03		0.17	0.48	0.32		6.99		3.55	3.44	0.60	1.70	1.13		
A W	73	Chronic simple glaucoma	1.22		0.11	0.38	0.30										
S B	52	Secondary glaucoma	1.58		0.11	0.30	0.22		6.54		4.01	2.53	0.44	1.20	0.88		
H R	54	Secondary glaucoma	1.06		0.17	0.29	0.47		7.20		3.70	3.50	0.63	1.07	1.74		
R Mc	53	Acute glaucoma	1.12		0.23	0.27	0.30		7.20		3.80	3.40	0.87	1.03	1.48		
W S	62	Acute glaucoma	1.26		0.07	0.46	0.26		6.43		3.53	2.85	0.25	1.65	0.93		
M M	71	Acute glaucoma	1.17		0.20	0.35	0.30		6.60		3.56	3.04	0.71	1.24	1.07		
F S	47	Chronic iridocyclitis	1.41		0.23	0.25	0.22		6.70		3.92	2.78	0.80	0.98	0.86		
N D	61	Chronic iridocyclitis	1.98		0.08	0.21	0.21		6.40		4.25	2.15	0.34	0.89	0.89		
D N	72	Vogt Koynagi disease	1.10		0.21	0.33	0.37		7.67		4.02	3.65	0.84	1.33	1.49		
M C	65	Cortical cataract	1.18		0.20	0.27	0.37		6.46		3.48	3.00	0.65	0.94	1.29		
A D	67	Sympathetic ophthalmia	1.20		0.12	0.35	0.36		6.04		3.29	2.75	0.39	1.25	1.28		
P S	66	Macular degeneration	1.84		0.08	0.23	0.24		6.20		4.02	2.18	0.32	0.92	0.96		
Normal serum			1.99		0.12	0.21	0.10		7.00		4.67	2.33	0.56	0.98	0.87		
Standard deviation			±0.3		±0.025	±0.04	±0.04										

* Values are expressed in grams per hundred cubic centimeters

more specific changes. An attempt was made to select patients with uncomplicated ocular disease, but with conditions such as glaucoma the absence of other pathologic processes is rare.

Consideration of the data in the table shows that significant changes were found in all the patients studied except for 1 with chronic iridocyclitis (case 61) and another with macular degeneration (case 66). Changes occurred in all the fractions, with no apparent correlation between the alteration in any fraction or fractions and the type of pathologic process present.

A more startling change was found in the diagrams of the ascending boundaries of serums of all the patients except the one with macular degeneration (case 66). Typical diagrams of ascending and descending boundaries found with the various



Diagrams of ascending and descending boundaries for the serums of patients with various ocular diseases and for normal serum

pathologic conditions are presented in the figure, with the patterns of normal serum for comparison.

In all of the ascending patterns the beta boundary is composed of two or more fractions. In the pattern for chronic simple glaucoma there are three peaks at the position of the beta boundary, and an additional boundary appears between the beta and the gamma fraction. In the patterns for secondary glaucoma and acute glaucoma, the beta boundary on the ascending side is clearly separated into two fractions, and the boundary on the descending side also shows a splitting of this fraction. The ascending patterns for serums of patients with other pathologic conditions show the new β peaks to varying extents. It is noteworthy that the serum of the patient (case 61) with chronic iridocyclitis, which gave normal protein concentrations, clearly shows the changes in the beta boundary.

COMMENT

Ocular disease cannot definitely be held responsible for the significant changes in the concentrations of the protein fractions in the serum of the patients studied because of the existence of other pathologic conditions which might complicate the picture. However, the appearance of new fractions in the beta boundary may be assigned to the ocular lesion with more certainty because of the failure of other investigators to find these changes associated with a large number of other pathologic conditions. The appearance of new protein fractions seems to be a characteristic observation in cases of chronic intraocular disease.

It is possible that this alteration in the serum protein picture is caused by the elaboration of a new fraction by the body in response to some antigen originating in the eye. In all probability, this antigen is either uveal pigment or lens protein, since these substances are the only homologous antigens which have been demonstrated in the eye. The appearance of the new fraction with conditions in which the lens is thought not to be involved suggests that the pigment is the more important factor.

The reason for the absence of the new boundary or boundaries on the descending side of the diagram of a number of serums is not known. Its presence on the descending side in certain of the serums indicates that the change might appear in all diagrams on more prolonged electrophoresis, but the possibility that this alteration is due to the breaking of some complex in the beta boundary must be considered.

Further work on the entire problem is in progress.

SUMMARY

Electrophoretic analyses of the serums of patients with various ocular diseases have been made.

Significant changes in the concentration of the electrophoretic fractions have been found. These changes did not appear to be characteristic of any given ocular condition.

A new boundary with a mobility between that of alpha and that of beta globulin appeared in the ascending pattern of serums of patients with chronic glaucoma, iridocyclitis and sympathetic ophthalmia.

Slight indications of the new fraction in the serum of patients with secondary glaucoma following extracapsular extraction and cortical cataract were found.

The possible relation of the changes in the protein of the serum to sensitization is discussed.

The electrophoretic equipment used in this study was constructed with funds furnished by the Abbott Research Foundation of Northwestern University and the American Association for the Advancement of Science.

Dr. S. R. Gifford gave advice and aid in this study.

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A NEW OPHTHALMIC IMPRESSION MATERIAL

THEODORE E OBRIG, B A

NEW YORK

The satisfactory fitting of contact lenses became a possibility when J Dallos, in 1933, discovered the feasibility of making molds of the living human eye with Pollner's negocoll

The disadvantages of the use of negocoll involve primarily physical factors, such as the time consumed in preparation. The boiling for liquefaction takes almost an hour. The hot liquid negocoll must be transported in a thermos jar and subsequently cooled in a glass beaker. With constant agitation with a stirring thermometer, it is cooled to an exact temperature, at which it must be immediately placed on the eye. The slight chemosis produced by the heat of the liquid negocoll (106 F) and the slight sting experienced by the patient after the mold has been removed, while not of much consequence, are also undesirable.

One of my students, who has made a hobby of contact lenses, observed a technic for the molding of living tissues other than the eye. This drew his attention to a preparation which he believed would be superior to negocoll. He sent an experimental quantity of this material to me and to Miss Gertrud Salvatori, who has made several thousand contact molds. She immediately began clinical experimentation. During the early months of her work, facts were uncovered which necessitated changes in the formula of the molding material as originally submitted. With the cooperation of the manufacturing chemists, the present formula of the new molding powder was attained in the summer of 1942.

As soon as the basic experimental work was completed, the finished product was demonstrated to me. I immediately verified the observations of Miss Salvatori and have used the new molding powder for six months.

After 500 clinical patients had been observed and studied under medical supervision, the new molding preparation was released for general use under the name moldite powder.¹ It is an alginate gelling agent which reacts when mixed with distilled water. The gelling is retarded by a preparation which gives sufficient time for the material to be placed on the eye and the molding shell centered before the gelling takes place.

The advantages of moldite powder over negocoll may be stated as follows:

- 1 Heating utensils, thermometer, thermos bottle and beakers are eliminated.
- 2 The preparation is simple, the powder is merely mixed with distilled water and the mixture spatulated for two minutes.
- 3 The setting time can be regulated by variation of the temperature of the water and the time of spatulation. Warm water causes more rapid gelling, cold water retards gelling.
- 4 This material remains in a flowing state for about four minutes from the time it is first mixed with distilled water at room temperature. This latent period before actual gelling, is valuable in that it gives the eye time to become fixed in

¹ This is a product of secret composition, according to the author, the manufacturer refuses to provide the formula for it.

a state of rest and also allows any alteration of the position of the casting shell without the production of conjunctival wrinkling

5 The gelling process starts abruptly and continues rapidly to completion in about thirty seconds. In cases of nystagmus this feature is important

6 When the casting shell is removed, it is immediately evident that the moldite separates very readily from the eye and that manipulation of the upper lid is not necessary

7 The elasticity of the preparation is such that particles of the gel seldom break off and remain in the fornices. This eliminates any manipulation by instrument or other means to remove foreign bodies. A simple irrigation is sufficient

8 After the casting is completed, the eye appears normal, with slight signs of irritation, as evidenced by the absence of conjunctival injection, chemosis, tearing and photophobia

9 The patient does not complain of burning, stinging or other disagreeable symptoms

10 There is no greater blurring of vision or alteration of visual acuity than would be experienced from a similar instillation of local anesthetic and epinephrine

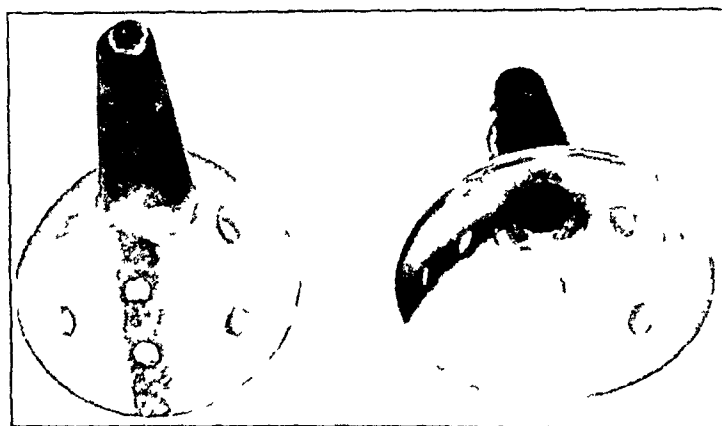


Fig 1—Perforated plastic casting shells

without the molding. The slight blur which is occasionally experienced disappears in half an hour

TECHNIC

The technic of making a mold of the human eye in moldite is simple and rapid. The equipment necessary consists of two rubber bowls (one for the moldite and one for the dental stone), one spatula, two casting shells, one wide-mouthed 10 cc graduate, one cylinder 10 cc graduate, moldite powder, dental stone (castite is best), distilled water, and a muscle hook.²

For a rapid, successful molding, the patient should be prepared both physically and mentally in order to insure his active cooperation.

To quiet his imagination, the entire procedure should be described briefly. The only instrument to be used near his eyes, the muscle hook, should be shown him with the comment that it is nothing but a bent piece of well rounded wire, with no sharp edges. As trial contact lenses have already been applied, he should be told that the molding is no more disagreeable than the insertion of these lenses.

It should be forcefully stated that the successful completion of the molding depends on his cooperation, principally in four ways. First, he must keep the eye not being worked on open and gazing at a predetermined point in order to center the cornea properly, second, he must keep his eyes quiet and fixed on this point for the second two minutes at least,

² The equipment described in this article can be obtained from the Obrig Laboratories, Inc., 49 East Fifty-First Street, New York

third, he must move his eyes as he is directed when the mold is being removed, and, fourth, he must keep his eyes wide open at all times and must not squeeze his lids down at any time during the process. Actually, all this is simple, and it is seldom that a patient gives any trouble. If he squeezes down the lids, the operator should stop work until he relaxes them again. No harm can come if the moldite and the casting shell on the eye are left for a short time. The operator should take his time and work deliberately and according to routine.

The casting shell which I use at present is the product of a gradual modification of the original glass molding shell designed seven years ago. Within the year important changes have been made which add considerably to its efficiency. The present solution of the problem is a plastic molding shell 24 by 27 mm. It has much the shape of an eye cup, with the flat base removed. The depth of the shell from the shallowest portion of the arched edge to the integral hollow handle is approximately 10 mm. The handle is 25 mm long, slightly tapered, completely hollow and open at the end. The shell wall is pierced with multiple perforations about 1 mm in diameter. These perforations, in conjunction with the hollow handle, allow the excess moldite gel to escape as the shell is placed on the eye, any pressure

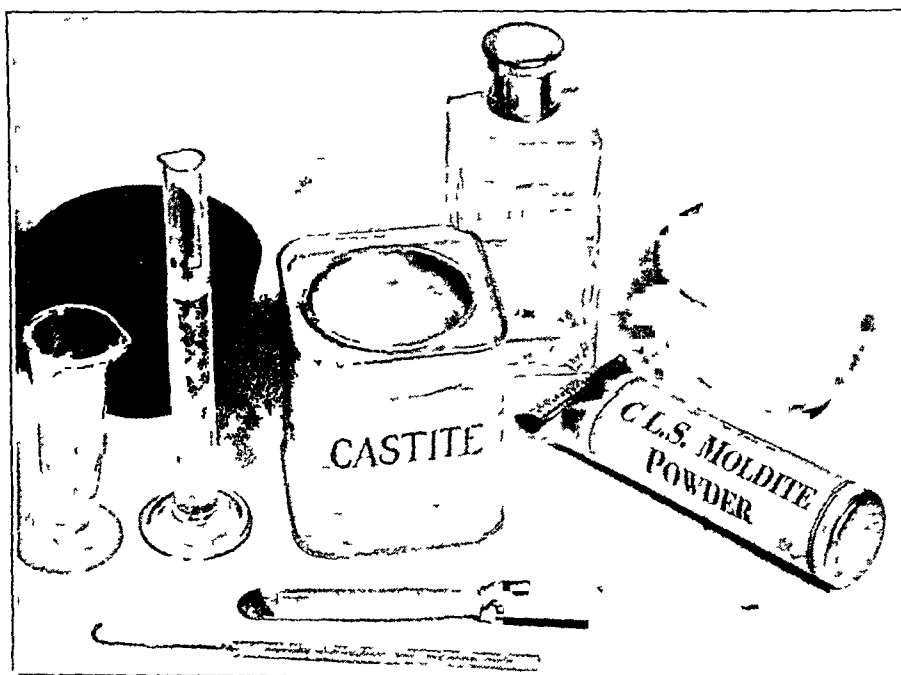


Fig 2—Simplified equipment for the making of molds of the eye with moldite

on the eyeball being thus eliminated. The perforations further prevent the loosening and separation of the moldite from the casting shell during its removal from the eye by affording it firm anchorage.

One of the long ends and the handle of the shell are marked with a red line to indicate the position of the right nasal side (red for right). Green markings are placed on the shell used for the left eye.

The patient should have thorough anesthetization of the conjunctiva and cornea with a 0.5 per cent solution of pontocaine hydrochloride. Two drops of the anesthetic is placed in each eye five minutes before the moldite powder is mixed. Two minutes should elapse before the second drop is instilled. A third drop may be instilled in the eye for which the cast is to be made when spatulation is begun. A minute later a fourth drop of anesthetic and 1 drop of epinephrine hydrochloride (1:1,000) are instilled.

The patient is placed in a supine position in a treatment chair or on a table, the operator making sure that the head is in a comfortable position, the procedure is then as follows:

1. Ten cubic centimeters of moldite powder is measured out in the wide-mouthed graduate and 7 cc of distilled water in the cylinder graduate. The powder and water are mixed in a small rubber bowl and spatulated to a smooth creamy mixture, about the consistency of face cream, the process being continued for two minutes.

2 The patient is instructed to fix his gaze so that the eye for which the cast is first to be made (usually the right) is turned so that the lower edge of the iris is at the level of the lower lid down and slightly to the nasal side. The upper and temporal scleral areas are the most important in a good mold.

3 The operator should work from back of the patient's head rather than from the side.

4 The assistant should dry both lids.

5 The moldite is scooped up on the spatula and the mixture placed in the casting shell.

6 The casting shell is held concave side up in the right hand, with the line marking the inner canthus facing toward the outer canthus, so that when the shell is turned over to be placed on the eye the mark will be directed nasally.

7 The upper lid is seized with the index finger of the left hand, the finger being parallel with not at 90 degrees to the margin of the lid. This gives better traction. The lid is retracted as far back as possible. The assistant retracts the lower lid at the same time, with a piece of gauze over his finger to insure traction.

8 The casting shell with the moldite is turned over and placed under the upper lid with the canthus mark turned up in the right eye and down in the left eye. Pressure is exerted against the upper lid, contact with the cornea being avoided. The whole shell is then rotated clockwise, so that the marking line is turned to the inner canthus and the shell slipped down under the lower lid. If the operator misses getting the shell under the upper lid, he should not work where the spilled moldite keeps him from seeing what he is doing. The shell should be removed, the moldite allowed to set, the material removed, the eye washed out and the process started over again. If the lower lid does not slip over the casting shell at first, the assistant should push up on the handle of the casting shell and retract the lower lid once more with a piece of gauze over his finger to give traction.

9 As soon as the casting shell is on the eye, the lids are released. The handle of the shell should not be held. The assistant may run his fingers up over the edge of the lower lid to make sure that it is over the casting shell. The margin of the lid cannot be seen because of the overflowing moldite.

10 The excess moldite should not be wiped away. As much as possible is spilled on the lids and lashes. It acts as a splint.

11 The patient must keep the free eye wide open and steady, without blinking if possible. This should be comparatively easy because of the anesthesia. No reflex due to drying of the cornea is likely to occur.

12 Five minutes from the time the powder and water are mixed the moldite will gel on the eye. The gel on the outside of the eye is then removed. First, the lashes of the upper lid are pulled out of the moldite with the muscle hook. Then the edges of the moldite gel are loosened from the lids, the cheek and the region of the inner canthus. If the entire mass is carefully worked and raised with the index finger and the hook, it will all come off in one piece. The operator should not be concerned, however, if it must be removed in a number of pieces. He should take his time, no discomfort is given the patient.

13 The patient is instructed to look up toward the operator as far as possible. The lower lid is retracted with the index or the second finger of the left hand. Firm pressure is directed upward on the handle of the casting shell with the thumb or the index finger of the same hand, and it is forced gently toward the eyebrow. With the muscle hook in the right hand, the operator gently stretches the folds of the bulbar conjunctiva downward and away from the casting shell with the portion of the hook forming the rounded angle. At the same time slight pressure is exerted on the sclera until air is heard or felt to enter under the casting.

14 The patient is instructed to look down and the casting shell is removed, slight pressure being maintained against the upper lid as the shell is pulled down and out.

15 The moldite mold is filled at once with fixing solution. This is important. The casting shell is placed, handle down, into a short, squat, narrow-mouthed bottle, such as that in which opticians obtain spectacle screws. The fixing solution is prepared from the white tablets supplied with the moldite powder. One tablet is dissolved in 200 cc of water. The fixing solution should be kept in a conspicuously marked bottle, so that it will not be confused with the distilled water or come in contact with the eye.

16 The attending physician should now irrigate the eye thoroughly to remove any small particles which may have become detached from the outside of the casting shell.

17 The cast is made for the left eye with the same technic except that no anesthetic is instilled into the right eye. Two instillations into the left eye of the anesthetic and one of the epinephrine solution is all that is necessary.

18 With both negative molds completed and filled with fixing solution, about $\frac{1}{2}$ inch (1.27 cm) of water is poured into the second rubber bowl and sufficient castite (hard dental stone) sprinkled on with the spatula to absorb all the water, and then a bit more is added. This mixture is spatulated well. The bowl is tapped to force any air bubbles to the surface. The dental stone is mixed as thick as possible, but thin enough that it will flow.

19 The fixing solution is poured out of the negative mold and the mold dried lightly with a piece of cotton.

20 The dental stone is poured into the negative mold from the side, without contact with the moldite gel or the casting shell. One can do this by pressing the rubber bowl into a spout and alternately pressing on and releasing the spout, so that the stone is forced into the mold. If castite is used, it will level off with no attention.

21 The stone is allowed to harden for about a half-hour.

22 With a stylus or a pencil with a sharp point, a horizontal line is drawn from the inner to the outer canthus. The operator holds the casting as if he had just removed it from his own eye, with the inner canthus mark directed toward his own inner canthus. Then, above the horizontal line, in the center, an *R* is engraved for the right eye and an *L* for the left eye, an *N* is engraved to the nasal side, and a *T* to the temporal side. Below the line the patient's name is engraved, thus

$$\begin{array}{c} \text{TLN} \\ \hline \text{Jones} \end{array}$$

$$\begin{array}{c} \text{NRT} \\ \hline \text{Jones} \end{array}$$

23 In about an hour the positive cast is separated from the negative mold. If castite stone is used, this is easy.

49 East Fifty-First Street

EFFECT OF SULFONAMIDE OINTMENT ON HEALING OF EXPERIMENTAL WOUNDS OF RABBIT CORNEA

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PAUL F DE GARA, M D
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The local treatment of various infective processes of the eye with sulfonamide compounds has been reported, but the results obtained have not been uniform¹ According to Bellows,^{1c} topical application of sulfonamide compounds is "effective in pyogenic dermatoses, infectious blepharitis, inclusion blennorrhea, and some forms of acute conjunctivitis" These substances also have been used locally in prophylactic treatment and in therapy of open surgical wounds subject to contamination with micro-organisms² According to Long³ "sulfonamide ointments are of value in the treatment of infected wounds" The local application of crystalline sulfonamide compounds has been recommended for the treatment of war wounds, in which infections with gas bacilli, staphylococci or hemolytic streptococci are likely to occur⁴ Recently, the use of sulfanilamide and its derivatives, either in the form of powders or incorporated in ointments, has been suggested for the treatment of fractures of the orbital walls and of burns of the eyelids or the anterior portion of the eyeball⁵

Experimental studies with sulfonamide compounds on the eyes of rabbits were first made by Rambo⁶ He showed that these compounds can be safely used in the conjunctival sac as a saturated aqueous solution, as a very fine powder or as a

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5 per cent suspension in olive oil. Injection of 0.02 Gm. of sulfanilamide in aqueous suspension into 4 eyes infected with streptococci resulted in complete healing of 3 eyes and in a delay of the infectious process in the fourth, while 4 untreated control eyes became purulent within four days. Sulfanilamide applied in ointment form readily penetrated the normal cornea of the rabbit,⁷ but other sulfonamide compounds (sulfapyridine, sulfathiazole and sulfadiazine) were recovered from the aqueous only in small quantities. Powdered sulfanilamide applied to the conjunctival sac of the rabbit resulted in a considerably higher concentration in the aqueous than that produced by the salve. However, there was slight damage to the corneal epithelium, which may have increased its permeability to the powdered form of the drug.

According to Vail,⁸ "the local use of sulfanilamide ointment or powder, in external ocular lesions particularly, is worthy of further trials and studies and is of much promise." Ointments containing sulfonamide compounds in approximately 5 per cent concentration have been employed in the treatment of ocular infections.⁹ Because of the apparent growing importance of these substances in the treatment of civilian and military war wounds, it seemed desirable to study the effect of local treatment with an ointment containing 5 per cent of sulfonamide compounds on the healing of experimental wounds of the cornea of rabbits. The wounds were produced (*a*) with sterile instruments (Graefe's knives, wide keratomes, Hippel's trephines) and (*b*) with similar instruments previously infected with hemolytic staphylococci.

MATERIALS AND METHODS

Animals—Male albino rabbits, weighing 2,000 to 2,500 Gm., were used. The animals were anesthetized by an intravenous injection of pentobarbital sodium, supplemented with topical instillation of 1 per cent butacaine sulfate into the conjunctival sac.

Experimental Wounds—The following types of wounds were produced in the cornea:

A. Incised wounds causing no substantial loss of the corneal tissue.

1. Superficial lesions, measuring approximately 4 mm. in length and 0.4 mm. in depth involving the outer layers of the cornea but not penetrating Descemet's membrane.

2. Deep lesions, measuring approximately 5 mm. in length, perforating Descemet's membrane and penetrating the anterior chamber.

B. Incised wounds causing substantial loss of the corneal tissue. These wounds were produced with a guarded trephine and are designated as "trephine wounds."

1. Superficial trephine wounds, with removal of a cylindric portion of the corneal tissue measuring approximately 3 mm. in diameter and 0.4 mm. in depth. This section of the cornea did not involve Descemet's membrane.

2. Deep trephine wounds, producing a punched-out lesion measuring approximately 1.5 mm. in diameter, perforating Descemet's membrane and penetrating the anterior chamber.

Infection—A twenty-four hour broth culture of *Staphylococcus aureus* haemolyticus was freshly diluted with sterile broth (1:10). The instruments were immersed for two minutes into the diluted culture and then used immediately to produce the different types of wounds of the cornea. This micro-organism was selected because of its frequent occurrence in infected ocular wounds.

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8 Vail, D. J. Sulfanilamide Compounds in Ophthalmology, editorial, *Am. J. Ophth.* **24**: 339-341 (March) 1941.

9 Guyton, J. S. Local Use of Sulfanilamide Compounds in the Eye, *Am. J. Ophth.* **24**: 292-297 (March) 1941.

Treatment—A 5 per cent sulfanilamide ointment and a 5 per cent sulfadiazine ointment were prepared according to Guyton's formula^{9a}. Equal parts of the two preparations were mixed and used in amounts of approximately 0.1 Gm.

Of the two compounds, sulfanilamide is "the drug of choice" for topical use in wounds because of its known antibacterial activity and its high solubility and diffusibility and because it appears to be the least harmful to regenerating tissues of the commonly used sulfonamide compounds. The addition of sulfadiazine, which is equally antibacterial but which is absorbed and excreted more slowly than sulfanilamide, was made to obtain a prolonged chemotherapeutic effect.

Time of Treatment—The first local treatment was given shortly after the production of the wound, usually at 9 a. m., a second application of ointment was made at 1 p. m. and a third at 5 p. m. Thereafter, local treatment was continued every day at 9 a. m., 1 p. m. and 5 p. m. until the eye showed clinical signs of healing. If the condition of the eye did not improve within two weeks, treatment was discontinued.

Clinical Examination of the Eyes—The eyes were examined each morning before application of the treatment. The cornea was examined with a magnifying device and with focal and diffuse illumination. The specular reflex was often observed. In addition, the eyes were stained with a 2 per cent solution of fluorescein sodium. The wound was considered clinically healed when the cornea did not stain with the dye and the other gross signs and symptoms of conjunctivitis, iritis and keratitis had subsided.

Laboratory Examinations—Material obtained with a sterile cotton swab from the corneal surface was examined before traumatization and repeatedly during the course of the treatment. Cultures were made on solid and in liquid mediums. Histologic studies were made on 39 eyes after the death of the animals. The eyes were fixed in Helly's fluid, and sections were stained with hematoxylin and eosin.

RESULTS

Experimental wounds were produced on 88 corneas. Three animals were killed within fifteen minutes after traumatization and the eyes preserved to illustrate the various types of lesions produced. Of the remaining 82 eyes, 32 were treated with the sulfonamide ointment, 17 received the ointment base without the sulfonamide compound and 33 were not treated.

Healing of Superficial and Deep Incised Wounds of the Cornea—A superficial incision of the cornea was produced with a sterile instrument on both eyes of 6 rabbits. Of the 12 eyes, 4 were treated with the sulfonamide ointment, 4 received the ointment base without the sulfonamide compound and 4 were not treated.

In a second group of 6 rabbits an incision penetrating into the anterior chamber of both eyes was produced with a sterile keratome. As in the first group, 4 eyes were treated with the sulfonamide ointment and 4 eyes with the ointment base alone, and 4 eyes received no treatment.

The results obtained on these 24 eyes are summarized in table 1.

There was no significant difference in the average healing time of superficial corneal lesions between the wounds treated with the sulfonamide ointment, the wounds treated with the ointment base alone and the wounds receiving no treatment. The average healing time of deep corneal incisions treated with sulfonamide ointment was considerably longer than that of the untreated control wounds. A similar delay in the healing process was also observed when the ointment base alone was used. Therefore, the retardation in the healing processes in this group cannot be attributed to the action of the sulfonamide compounds.

^{9a} Guyton⁹. The formula employed was as follows. Ten parts of the sulfonamide compound (sulfanilamide or sulfadiazine) was dissolved in 25 parts of boiling water, and 4 parts of sodium alginate, in 75 parts of boiling water. These solutions were mixed and stirred until cool. Sixteen parts of anhydrous wool fat, 1 part of sodium chloride dissolved in 4 parts of water and 78 parts of white petrolatum base were added to the sulfonamide-sodium alginate mixture and stirred until a smooth ointment was obtained.

A slight conjunctival reaction, lasting for approximately six hours after the traumatization, was the only clinical manifestation observed in some of the eyes with superficial incised wounds. When deep incisions penetrating into the anterior chamber were produced, a pronounced conjunctival reaction, with some discharge, and slight or moderate iritis were frequently noted. These reactions subsided within one to three days after the experimental incision. The anterior chamber was reformed in from six to twenty-four hours after the incision.

In a third group of 6 rabbits superficial and deep incised wounds of both corneas were produced with instruments infected with hemolytic staphylococci. Six eyes were treated with the sulfonamide ointment, and 6 eyes were not treated. The ointment base alone was not employed because it did not accelerate healing of noninfected wounds and therefore could not be expected to be effective in the presence of micro-organisms.

In this group, again, the tendency of the superficial wounds to heal was good. The average healing time of the eyes treated with sulfonamide ointment was 40 hours, and that of the untreated controls was 24 hours. A slight conjunctival reaction of short duration was the only clinical symptom in this group.

TABLE 1—*Effect of Local Treatment with Sulfonamide Ointment* on Healing Time of Superficial and Deep Noninfected Incised Wounds of the Cornea of Rabbits*

Type of Incised Wound	No. of Eyes	Treatment	Time of Healing, Hr.	Average Healing Time, hr.
Superficial	4	Sulfonamide ointment	22, 22, 24, 46	28.5
	4	Ointment base	22, 24, 30, 48	31
	4	None	24, 24, 24, 24	24
Deep	4	Sulfonamide ointment	24, 96, 96, 120	84
	4	Ointment base	24, 96, 96, 120	84
	4	None	24, 48, 48, 48	42

* Ointment containing sulfanilamide and sulfadiazine in 2.5 per cent concentration each.

Healing of deep incised infected wounds occurred in only 1 eye treated with the sulfonamide ointment for ten days. The other 5 eyes (2 treated and 3 untreated) became progressively worse. Within twenty-four hours after traumatization, inflammatory reactions of the cornea, conjunctiva and iris appeared. There was also considerable mucopurulent discharge. Keratitis, conjunctivitis and iritis became more evident during the next three to four days, and a hypopyon ulcer frequently developed. At this time the eyes presented marked to extensive conjunctivitis and keratitis, with pannus formation and ulceration of the cornea and moderate to severe iritis and uveitis. The end result was complete blindness from endophthalmitis or phthisis bulbi. The staining reactions remained positive throughout the course of the experiments.

Our observations on the effect of local treatment with a 5 per cent sulfonamide ointment on the healing time of incised experimental wounds of the cornea of rabbits gave the following results:

Superficial wounds, both noninfected and infected, healed in from 22 to 48 hours. The average healing time of the treated eyes and that of the untreated control eyes did not show significant differences.

Deep noninfected wounds healed in from 24 to 120 hours. The average healing time of the untreated control eyes was 42 hours, and that of the treated eyes was 84 hours. The sulfonamide ointment and the ointment base alone showed the same retarding effect on the average healing time, therefore, the retardation cannot be attributed to the action of the sulfonamide compounds. Healing of deep

infected wounds occurred in only 1 eye, which was treated with sulfonamide ointment for ten days. In the other 5 eyes (2 treated and 3 untreated) blindness developed from endophthalmitis or phthisis bulbi.

Healing of Superficial and Deep Trephine Wounds of the Cornea—A superficial trephine wound was produced with a sterile instrument on the cornea of both eyes of 7 rabbits. Of the 14 eyes, 5 were treated with the sulfonamide ointment, 5 received the ointment base alone and 4 were not treated.

In another group of 9 rabbits, a trephine wound perforating Descemet's membrane was produced with a sterile instrument in both eyes. Six eyes were treated with the sulfonamide ointment, 4 eyes received the ointment base alone and 8 eyes had no treatment.

The results obtained with these 32 eyes are given in table 2.

There was no significant difference in the average healing time of superficial trephine wounds of the cornea between the eyes treated with sulfonamide ointment and the untreated control eyes. The average healing time of the eyes treated with the ointment base alone was notably prolonged in 2 instances. Similarly, the differences in the average healing time of deep trephine wounds perforating Descemet's

TABLE 2—Effect of Local Treatment with Sulfonamide Ointment* on Healing Time of Superficial and Deep Noninfected Trephine Wounds of the Cornea of Rabbits

Type of Trephine Wound	No. of Eyes	Treatment	Time of Healing, Hr	Average Healing Time Hr
Superficial	5	Sulfonamide ointment	96, 96, 96, 120, 144	110.4
	5	Ointment base	96, 120, 192, 240, 264	182.4
	4	None	48, 120, 120, 192	120
Perforating	6	Sulfonamide ointment	48, 96, 144, 144, 168, 168	128
	4	Ointment base	120, 144, 144, 168	119
	8	None	96, 96, 96, 96, 120, 120, 120, 168	114

* Ointment containing sulfanilamide and sulfadiazine in 2.5 per cent concentration each.

membrane were slight. In the rabbits receiving the deep trephine wound, the untreated control eyes showed the shortest average healing time.

The clinical picture in the rabbits that had received trephine wounds of the cornea consisted in moderate to pronounced conjunctival reaction, with considerable mucopurulent discharge and varying degrees of keratitis and anterior uveitis. These symptoms usually appeared within a few hours after the injury, became more pronounced after twenty-four hours and gradually subsided.

Finally, superficial and deep trephine wounds were produced in the corneas of 7 rabbits with a trephine infected with hemolytic staphylococci. Seven eyes were treated with the sulfonamide ointment, and 7 eyes were not treated. The ointment base alone was not employed because no beneficial action on healing of the wounds could be expected from this ointment in the presence of micro-organisms.

In these animals, healing occurred after treatment with the sulfonamide ointment in 5 eyes (in 3, 3, 7, 9 and 14 days respectively) and without treatment in 3 eyes (in 3, 4 and 8 days respectively), while no improvement was seen in the remaining 6 eyes (2 with and 4 without treatment with the sulfonamide ointment). The clinical picture in this group showed more severe involvement of the conjunctiva, cornea and iris.

Local treatment with sulfonamide ointment of trephine wounds of the cornea of rabbits gave the following results:

The average healing time of superficial noninfected wounds of both treated eyes and untreated control eyes did not show significant differences, application of the ointment base alone retarded the healing considerably in 2 eyes

Deep noninfected wounds healed equally well whether the eyes were treated or were not treated

Healing of wounds produced with infected trephines occurred in 5 eyes after treatment with the sulfonamide ointment for periods varying from three to fourteen days and in 3 untreated control eyes. No healing was observed in 2 treated and in 4 untreated eyes

BACTERIOLOGIC STUDIES

A total of 143 cultures of material obtained from 48 eyes was examined. The material from the corneal surface before traumatization contained a variety of gram-positive and gram-negative micro-organisms, the most frequent being anhemolytic staphylococci, other gram-positive cocci and *Bacillus subtilis*. Essentially the same microbic flora was obtained in cultures of material obtained at daily intervals up to seven days after traumatization from both the treated and the untreated eyes. However, a notable inhibition of bacterial growth was observed in cultures of material from 8 of 24 eyes that had received treatment with sulfonamide ointment for one or two days. No inhibition of bacterial growth occurred in cultures of material from untreated eyes or from eyes receiving the ointment base alone.

Material from the corneal surface obtained a few minutes after traumatization of the eyes with instruments infected with *Staph aureus haemolyticus* yielded these organisms in pure culture. However, cultures of material taken after twenty-four and forty-eight hours from both the treated and the untreated eyes again contained the mixed bacterial flora previously described.

There was no evident relation between the healing time of the experimental wounds and the results of bacteriologic studies.

HISTOLOGIC STUDIES

Histologic studies were made on 39 eyes. Three rabbits were killed within fifteen minutes after traumatization in order to study the extent of the experimental wounds.

Photomicrographs of the two types of incised and trephine wounds, both superficial and deep, are shown in figures 1 to 4. It will be seen (figs 1 and 2) that the superficial wounds pierced the epithelium and Bowman's membrane and penetrated the corneal stroma but did not involve Descemet's membrane. The deep wounds (figs 3 and 4) involved all the layers of the cornea and penetrated the anterior chamber.

The histologic appearance of eyes which were considered "clinically healed" after receiving different types of experimental wounds of the cornea is illustrated in figures 5 to 12. The continuity of the epithelial layer covering the corneal surface was completely restored in every instance, this accounts for the lack of staining with the fluorescein solution.

Photomicrographs of 4 eyes which had received superficial incised or trephine wounds are shown in figures 5 to 8. These pictures were obtained at the time of "clinical healing," which occurred in from 24 to 192 hours. There was marked proliferation of the epithelium at the site of the previous injury. A slight degree of acute inflammation was seen in wounds produced with infected instruments (fig 6). In trephine wounds, which usually required a longer time for healing, the corneal stroma at the site of the previous injury appeared as a healed scar, containing fibroblasts and a few large macrophages (figs 7 and 8).

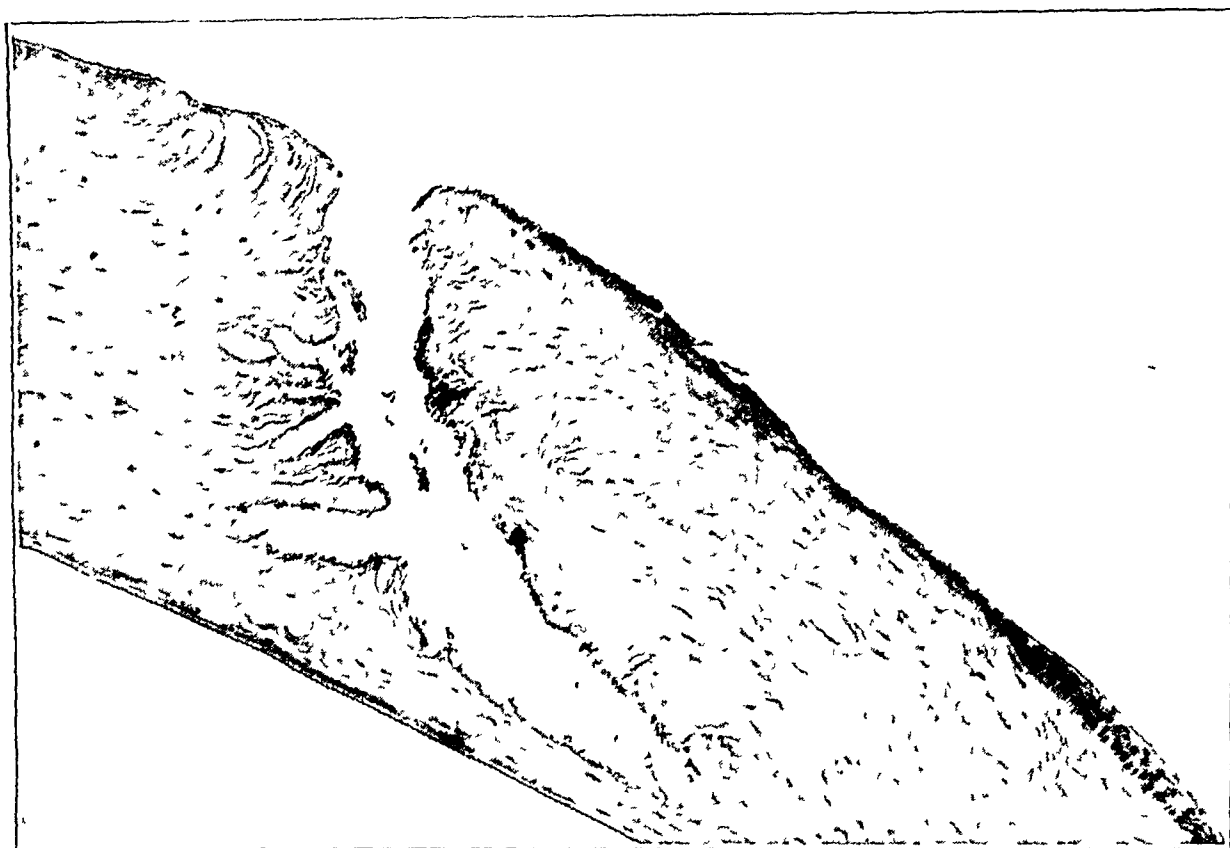


Fig 1—Extent of superficial incised wound in the rabbit's cornea The animal was killed within fifteen minutes after the injury $\times 120$

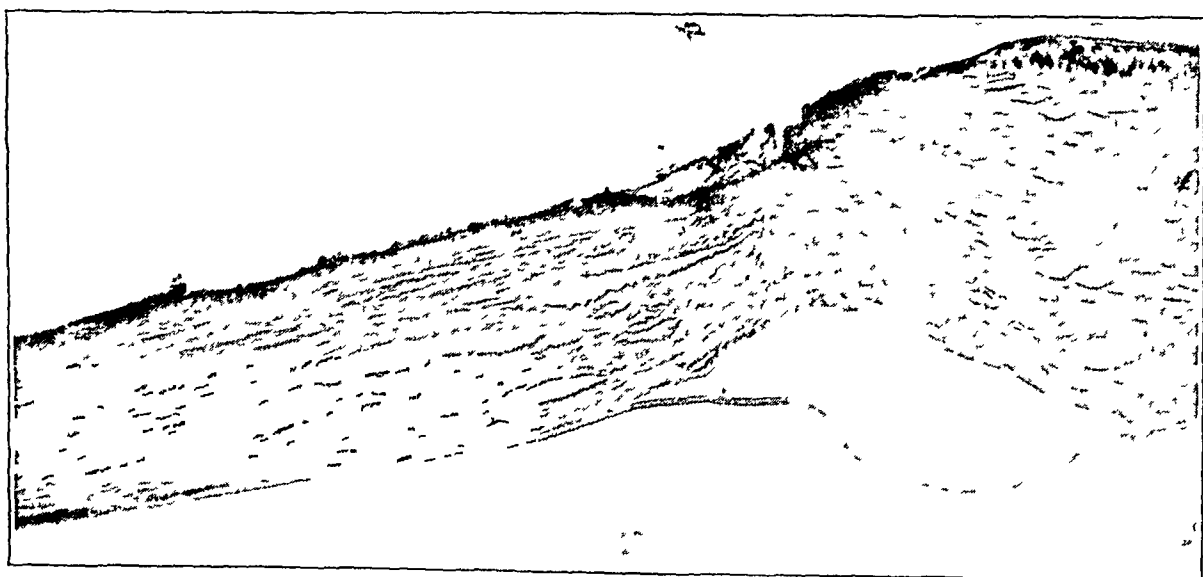


Fig 2—Extent of superficial trephine wound in the rabbit's cornea The animal was killed fifteen minutes after the injury $\times 120$

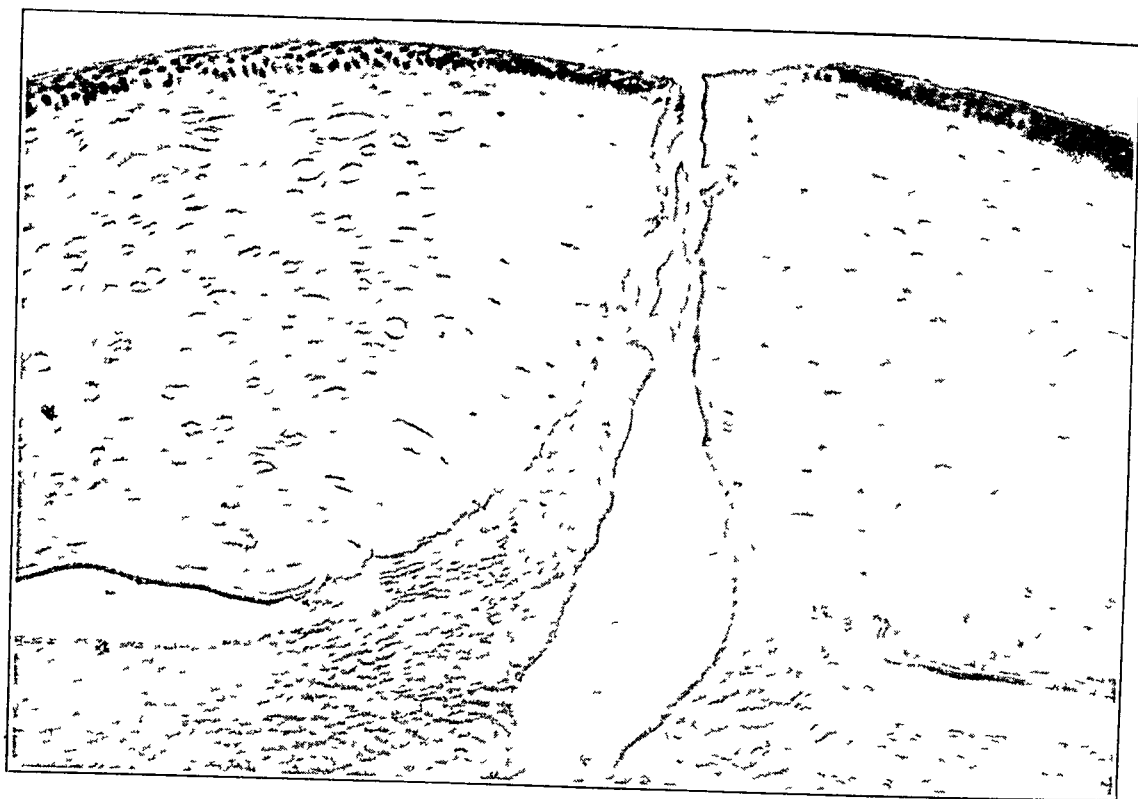


Fig 3—Extent of deep incised wound in the rabbit's cornea The animal was killed fifteen minutes after the injury $\times 120$

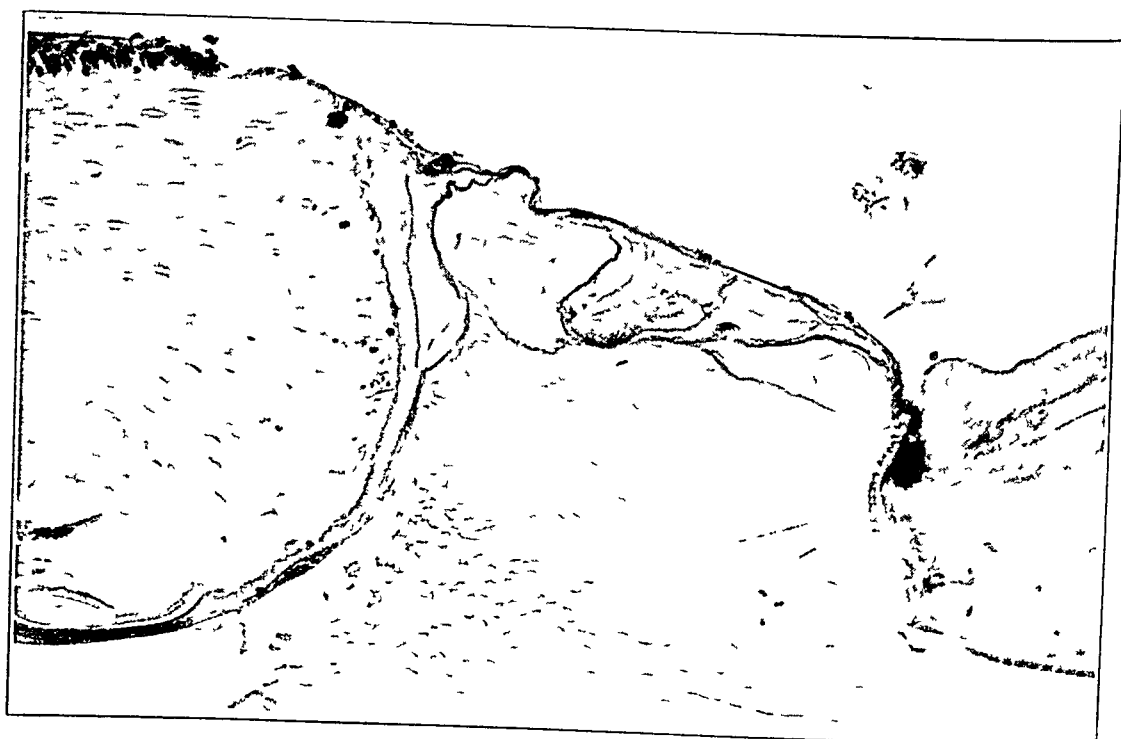


Fig 4—Extent of deep trephine wound in the rabbit's cornea The animal was killed fifteen minutes after the injury $\times 120$

The healing process of deep incised wounds showed thickening of the surface epithelium at the site of the injury, with ingrowth of the epithelium into the wound. The sections shown in figures 9 and 10 were obtained from the same eye at different levels, the corneal stroma still presents a gap in one section (fig 10), although the epithelium and endothelium apparently had already completely regenerated.

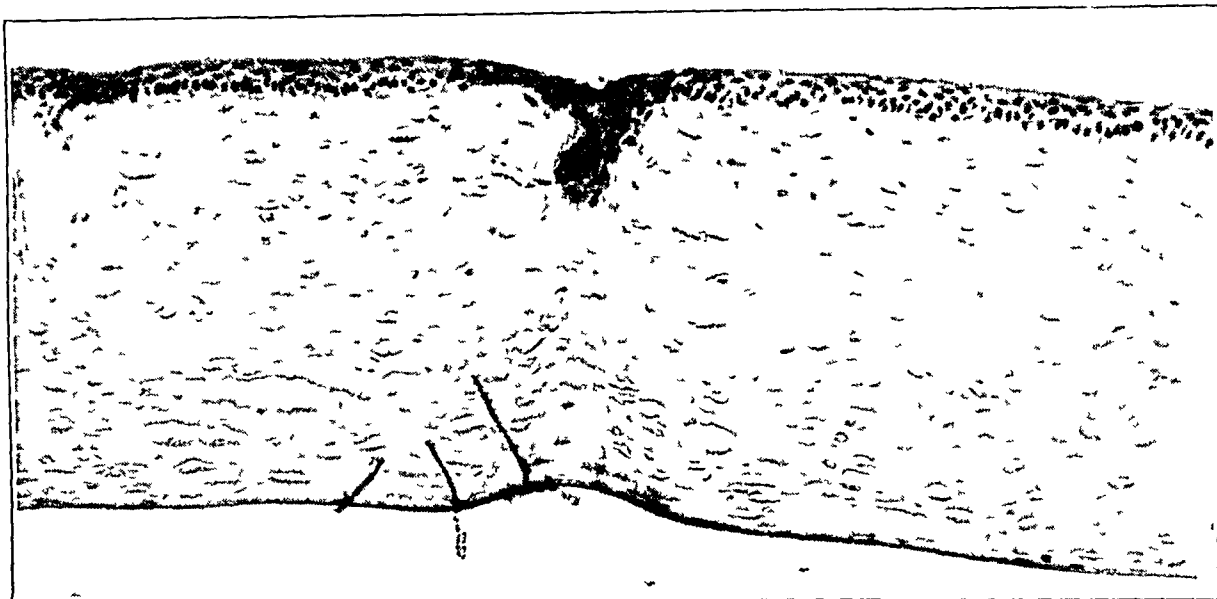


Fig 5—Healing of superficial incised wound in the rabbit's cornea produced with a sterile instrument, showing proliferation of regenerated epithelium. The eye was treated with an ointment containing sulfonamide compounds in 5 per cent concentration. The lesion healed in 24 hours, and the animal was killed eighteen hours later. $\times 120$

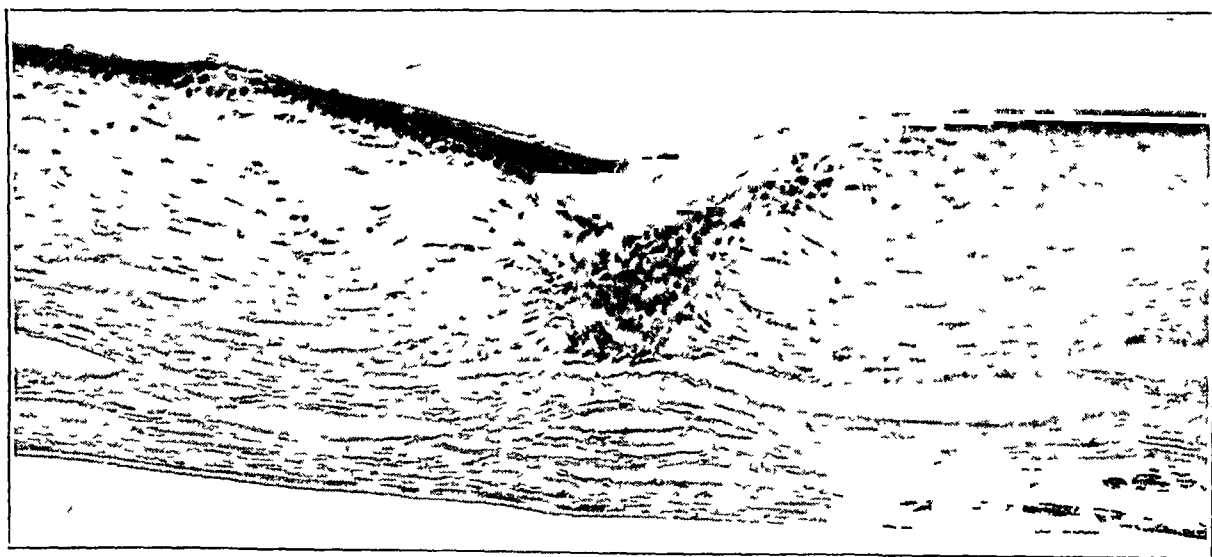


Fig 6—Healing of superficial incised wound in the rabbit's cornea produced with an infected instrument, showing thickening of regenerated epithelium and a slight degree of reactive inflammation. The lesion was treated with the sulfonamide ointment and healed in 24 hours. The animal was killed twenty-four hours later. $\times 120$

A typical scar with numerous fibroblasts was seen in eyes in which the healing time had been prolonged to 10 days after injury with an infected keratome (fig 11). The healing process of a deep trephine wound of a rabbit's cornea is shown in figure 12.

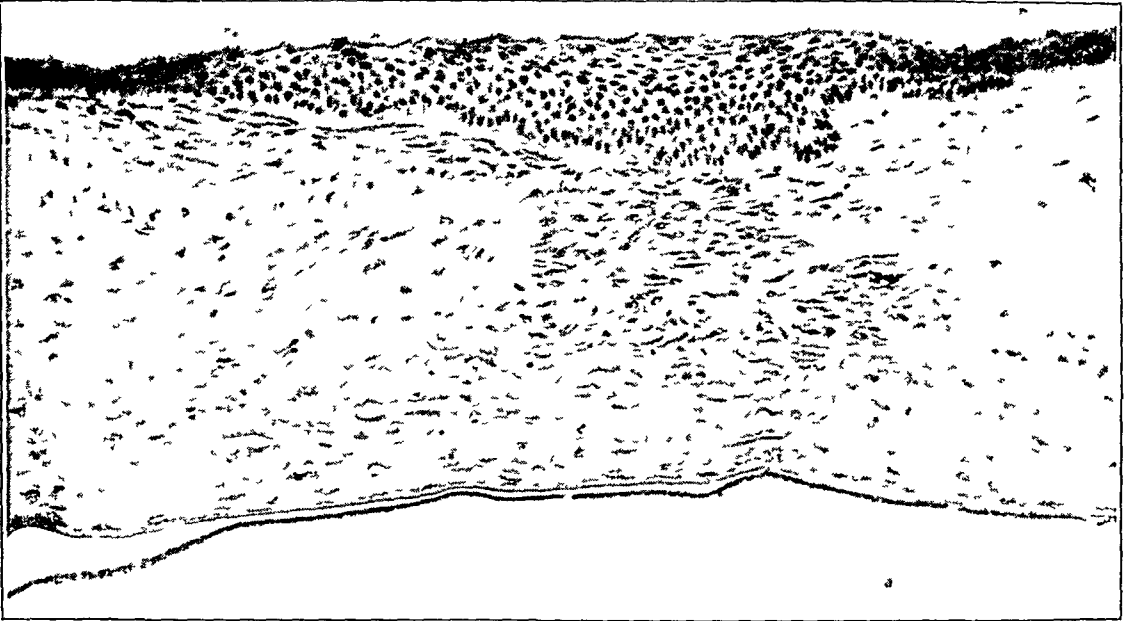


Fig 7—Healing of superficial trephine wound in the rabbit's cornea produced with a sterile instrument No treatment was administered The wound healed in 8 days $\times 120$

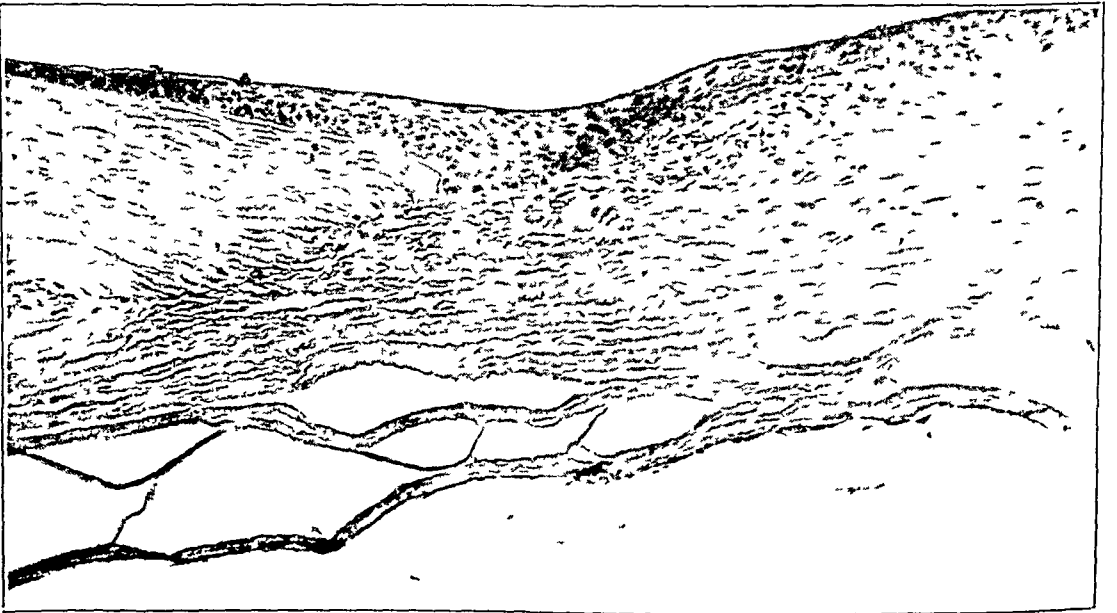


Fig 8—Scar following superficial trephine wound in the rabbit's cornea produced with an infected trephine The lesion, treated with the sulfonamide ointment, healed in 3 days The animal was killed twenty-four hours later $\times 120$

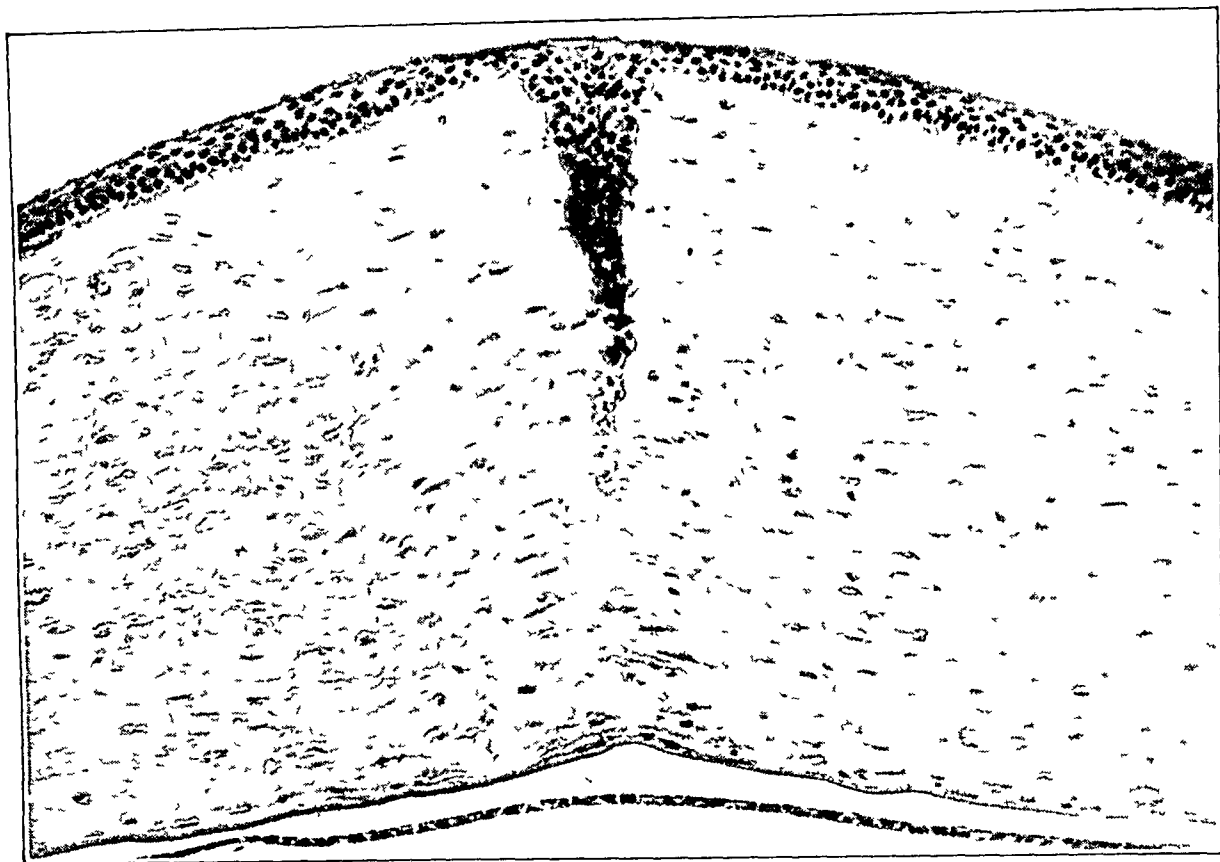


Fig 9—Healing of a perforating incision through Descemet's membrane of the rabbit's cornea produced with a sterile keratome, showing ingrowth of epithelium into the wound. No treatment was given. The wound healed in 24 hours, and the animal was killed eighteen hours later. $\times 120$

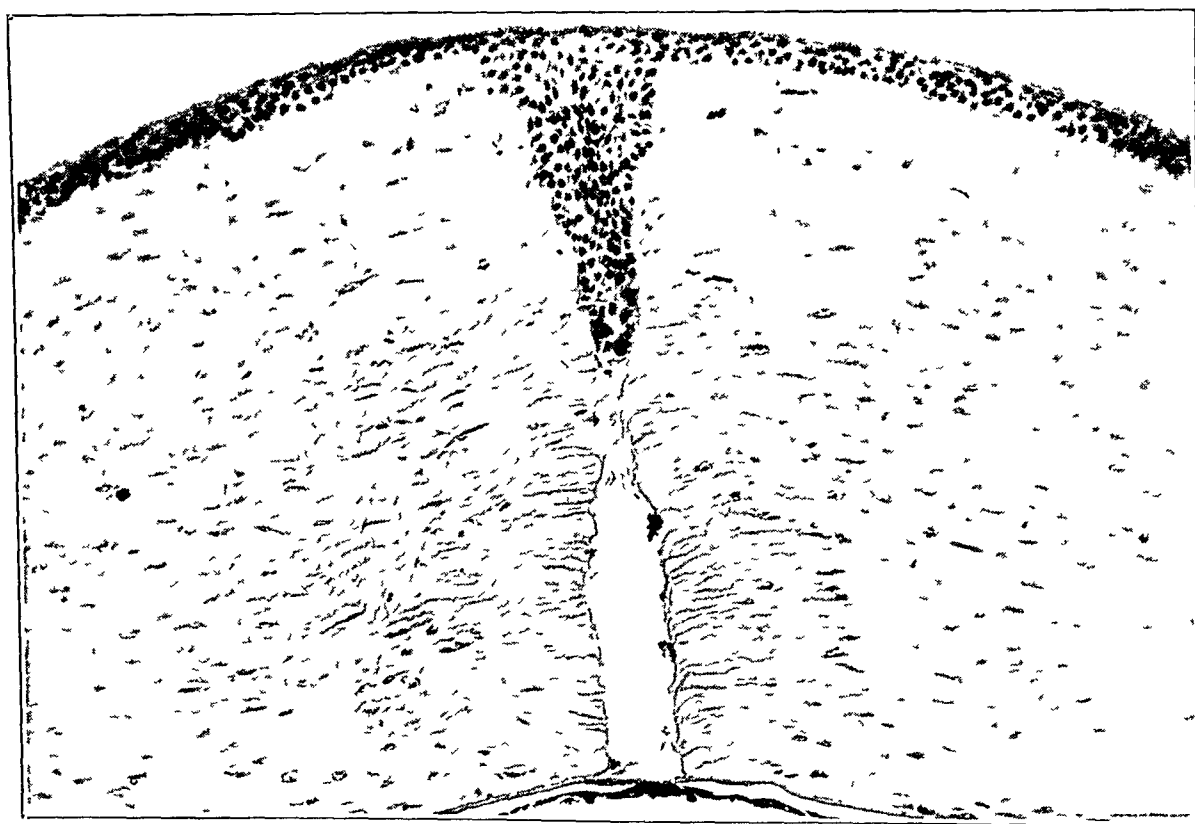


Fig 10—Another area of the cornea from the same eye from which the section shown in figure 9 was taken. Epithelial and endothelial regeneration is completed, but there is still a gap in the corneal stroma. $\times 120$

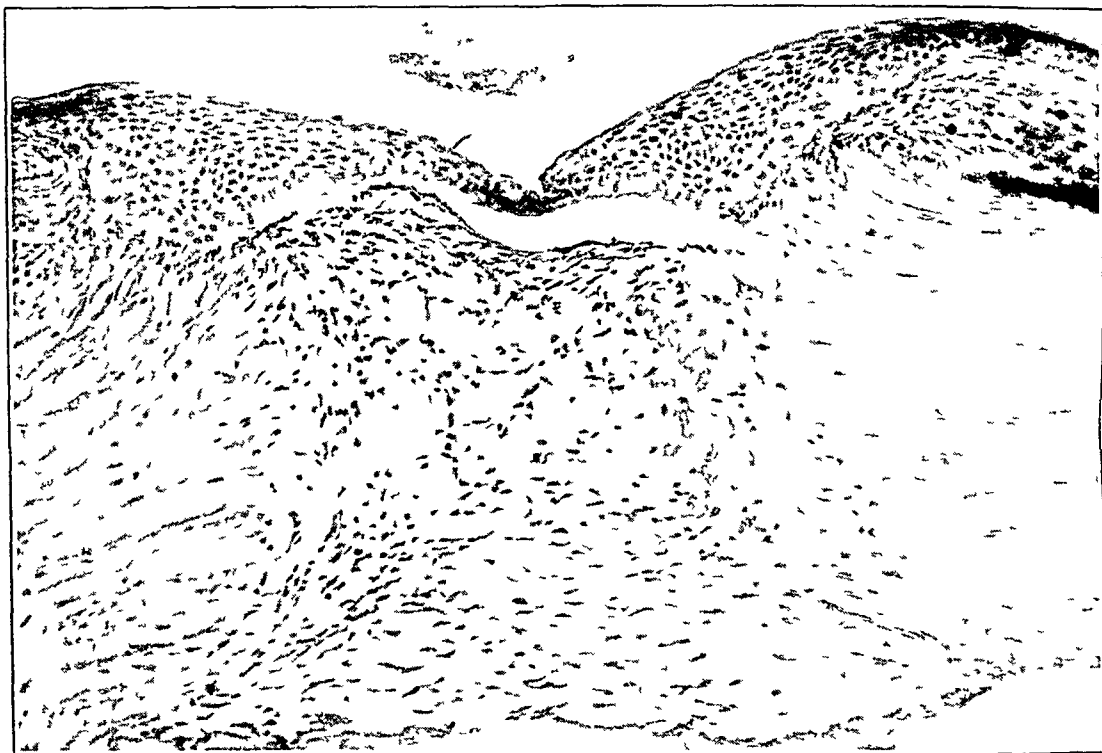


Fig 11—Scar following a deep incision produced in the rabbit's cornea with an infected instrument. The wound, treated with the sulfonamide ointment, healed in 10 days. $\times 120$

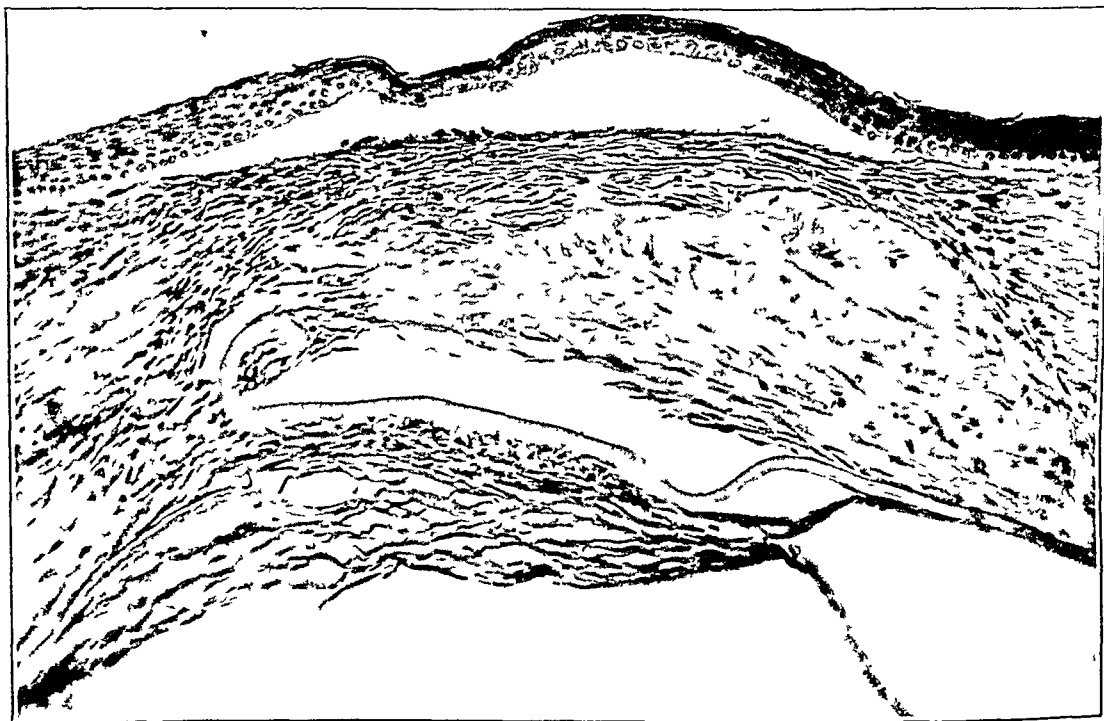


Fig 12—Healing of a deep trephine wound in the rabbit's cornea produced with an infected instrument. The lesion, treated with the sulfonamide ointment, healed in 7 days. $\times 120$

COMMENT

Healing of wounds in the presence of sulfonamide compounds is still a controversial question. Some investigators¹⁰ have reported retardation of the healing, and other workers¹¹ have observed no evidence of the interference of sulfanilamide with the process of normal healing. The local toxic effects of sulfonamide compounds on the ocular tissues have been recently investigated by Bellows and Gluckman¹². According to these authors, sulfonamide compounds cause severe damage to the cornea of rabbits in the absence of normal epithelium. The average healing time of the eyes treated with the sulfonamides was 51 days and that of the untreated control eyes was 13.3 days.

In our experience, the average healing time of corneal wounds produced with sterile instruments was usually somewhat prolonged in eyes treated locally with the sulfonamide ointment. This was especially noticeable in the eyes that received a deep incised wound (table 1). However, local treatment with the ointment base alone also retarded healing of the wound, frequently this retardation was greater than that observed in the eyes treated with the sulfonamide ointment. Therefore, our results do not permit the conclusion that the sulfonamide compounds were responsible for the delay in healing of the wound, but they indicate that the introduction of foreign material into a sterile wound may interfere with its healing.

In eyes that received experimental wounds with infected instruments the average healing time could not be determined because 11 of the 26 eyes did not heal but became progressively worse. Good results were observed with the sulfonamide ointment. In the eyes that had received trephine wounds with infected instruments, healing occurred in 5 of 7 eyes treated with the sulfonamide ointment and in only 3 of the 7 untreated control eyes. These figures are too small to be of statistical significance, but they apparently demonstrate the effectiveness of the sulfonamide ointment in treatment of infected corneal wounds.

Objection might be raised to our criteria for the determination of "clinical healing," namely the absence of staining with fluorescein and the regression of the inflammatory symptoms. However, at the stage of clinical healing the continuity of both the surface epithelium and the endothelial lining is completely restored, while the regeneration of the corneal stroma may still be incomplete (fig. 10). Since an intact epithelial surface offers protection against infection by invading micro-organisms, no further local treatment with sulfonamide compounds would be required. Therefore, the criteria employed were sufficient to determine the length of time that therapy with the sulfonamide compounds should be continued.

Local application of a 5 per cent sulfonamide ointment, containing equal amounts of sulfanilamide and sulfadiazine, usually did not accelerate the healing time of

10 Veal, J. R., Klepser, R. G., and De Vito, M. P. Preparation of Superficial Wounds for Skin Grafting by Local Use of Sulfanilamide and Sulfanilamide-Allantoin Ointment, *Am J Surg* **54** 716-720 (Dec.) 1941. Bick, E. M. Observation on the Topical Use of Sulfonamide Derivatives, *J. A. M. A.* **118** 511-513 (Feb. 14) 1942. Taylor, F. W. The Misuse of Sulfonamide Compounds, *ibid* **118** 959-961 (March 21) 1942.

11 Key, J. A., and Burford, T. H. The Local Implantation of Sulfanilamide in Compound Fractures, *South M. J.* **33** 449-455 (May) 1940. Harbison, S. P., and Key, J. A. Local Implantation of Sulfanilamide and Its Derivatives in Wounds. Its Relation to Wound Healing and to Peritoneal Adhesions, *Arch Surg* **44** 22-26 (Jan.) 1942. Klepser, R. G. Problems in the Local Use of Sulfonamides, *M. Ann. District of Columbia* **11** 211-213 (June) 1942.

12 Bellows, J. G., and Gluckman, R., cited by Bellows¹⁰.

experimental wounds produced with sterile instruments on the cornea of rabbits, its use, therefore, is of little therapeutic significance. This, of course, does not preclude the possibility that higher concentrations of sulfonamide compounds, a modification in the composition of the ointment or the local use of powdered sulfonamide compounds might not have a different effect and prove to be more useful than the sulfonamide ointment used in this series. Experimental work along these lines is in progress.

In agreement with Bellows,^{1c} our results indicate that the local use of the sulfonamide compounds can be limited at this time to cases in which chances of infection prevail. The results obtained with the sulfonamide ointment in our series of eyes with wounds produced with infected instruments are highly promising.

SUMMARY AND CONCLUSIONS

1 Superficial and deep wounds, with or without substantial loss of corneal tissue, produced with sterile instruments in the eyes of rabbits were treated locally with an ointment containing sulfonamide compounds in 5 per cent concentration (2.5 per cent sulfanilamide and 2.5 per cent sulfadiazine) and with the ointment base alone. The average healing times of the wounds of the cornea treated with the sulfonamide ointment and with the ointment base alone were usually greater than the average healing time of the untreated control eyes.

2 Healing of deep incised wounds produced with a keratome infected with *Staph aureus haemolyticus* occurred in 1 of 3 rabbit eyes treated with the sulfonamide ointment, but not in 3 untreated control eyes. Healing of trephine wounds produced with instruments infected with *Staph aureus haemolyticus* occurred in 5 of 7 eyes treated with sulfonamide ointment, but only in 3 of 7 control eyes.

3 Bacteriologic cultures of material obtained from the corneal surface of the eyes showed a mixture of gram-positive and gram-negative micro-organisms, staphylococci and *B subtilis* being the most frequently observed. A notable inhibition of the bacterial growth was observed in cultures of material from 8 of 24 eyes that had received treatment with the sulfonamide ointment but not in cultures of material from the control eyes. Essentially the same microbic flora was noted in cultures of material obtained at daily intervals during the process of healing. There was no demonstrable relation between the healing time of experimental corneal wounds and the bacterial flora.

4 Histologic sections of corneas of rabbits considered to be "clinically healed" revealed that the continuity of the surface epithelium was restored. There was pronounced thickening of the epithelium at the site of the previous injury. In wounds that required several days for healing, typical scar tissue was observed at the site of the previous wound. This was particularly noticeable in the wounds with infected instruments. Regeneration of the surface epithelium was observed at a time when the corneal stroma still presented lack of continuity.

5 Local use of an ointment containing sulfonamide compounds in 5 per cent concentration did not accelerate the healing of superficial or deep incised or trephine wounds of the cornea of rabbits if sterile instruments were used to produce the injury. The ointment was of value in the treatment of wounds produced with instruments that were infected with *Staph aureus haemolyticus*.

INFLUENCE OF PROLONGED WEARING OF MERIDIONAL SIZE LENSES ON SPATIAL LOCALIZATION

HERMANN M BURIAN, M D

HANOVER, N H

When a meridional size lens¹ is placed with its axis in the vertical position (at 90 degrees) in front of one eye of a normal observer, the retinal image of that eye is enlarged in the horizontal meridian. Since horizontal disparity of the retinal images is responsible for stereoscopic effects, the observer will experience typical changes in the appearance of his environment. If the size lens is placed in front of the right eye, objects located in the right half of the observer's field of vision appear larger yet farther away from him than objects of the same size situated at the same distances from the observer but located in the left half of his field of vision. A flat desk top will appear to be slanting down on the right side and slanting up on the left side, a wall perpendicular to the observer's line of gaze will appear farther away from him on the right side and closer to him on the left side, the ground on which the observer walks is tipped downward on the right and upward on the left side, as though he were walking on the side of a hill. If he holds his hands in front of his eyes, the right hand will seem to be larger. At the same time the shape of the objects will appear distorted. The top of the desk and the wall assume the form of a trapezoid, a square magazine lying on the right half of the desk, the form of a rectangle, and a round object, such as an ash tray or a round wash basin, the form of an ellipse. If the observer looks into a mirror he will find that his face has become asymmetric, with the right side protruding².

All spatial distortions produced by a size lens placed at axis 90 in front of one eye can be explained in a relatively simple manner, on a geometric basis. Assume that an observer's visual lines converge on a point F (fig 1) on a plane on which there are two points, P and N , seen in peripheral vision. Introduce now in front of the right eye a size lens which magnifies the horizontal meridian only. All distances are magnified for the right eye, and the distance PFN is increased to πFv . The object point P , originally imaged on the retinal point p_r in the right eye, now stimulates the more temporal point p'_r , the image of the object point N is displaced in the right eye from n_r to n'_r . No change in the image of the left eye has occurred. The horizontal disparity which is thus created results in a stereoscopic effect. Object point P appears to have advanced and object point N to have receded, since only points situated objectively at P' and N' could fulfil the condition of stimulating simultaneously the retinal elements p_1 , p'_r and n_1 , n'_r . As a result, the plane PFN appears rotated around the fixation point F . The

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1 These lenses have no appreciable refractive power but magnify the retinal image. They are ground as over-all size lenses, having the same magnification in all meridians, or as meridional size lenses, having a specified magnification in one meridian but no magnifying effect in the meridian at right angles. The designation of the axes and effective meridians of the size lenses is analogous to that of cylindric refractive lenses.

2 The importance of the relative size and shape of the ocular images in binocular spatial localization was recognized in the early stages of the research in aniseikonia. A full description of the result of new investigations will be given by A. Ames Jr. in publications now in preparation.

amount of rotation, as expressed by the angle Ψ , is proportional to the magnification introduced by the lens and is given by the formula $\tan \Psi = \left[\frac{M-1}{M+1} \right] \frac{b}{a}$, in which M is the magnification, b the fixation distance and a one-half the interpupillary distance.

The spatial distortions, although in the same direction for all normal observers, are not experienced in all environments and by all observers with the same intensity. Spatial orientation in man, particularly depth perception, is based on two groups of factors. One group can be derived only from the simultaneous stimulation of the two retinas, it comprises the psychophysiologic results produced by the stimulation of disparate retinal elements. They are designated as binocular or disparity factors. The other group can be obtained from the stimulation of one eye alone. It comprises such factors as perspective, size and form of known objects, the knowledge of what is level and what perpendicular, etc. These factors are the unocular

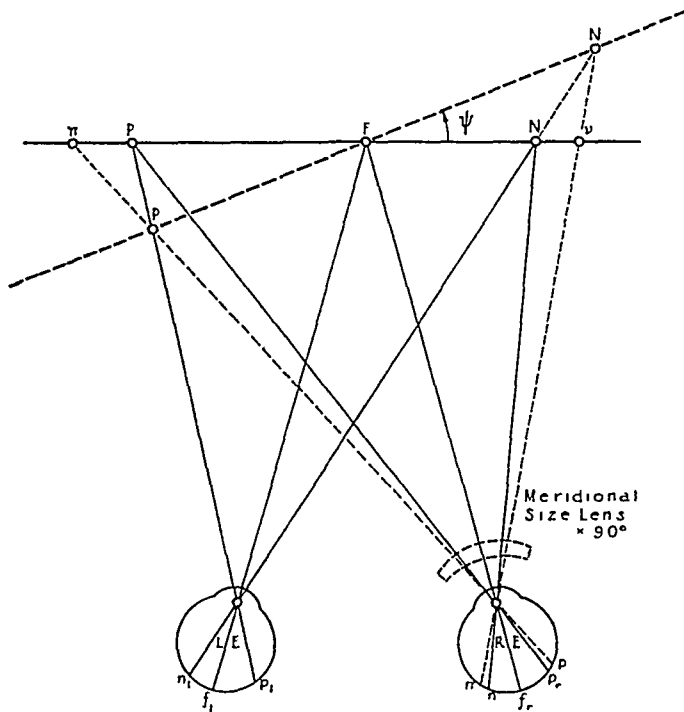


Fig 1—Apparent rotation of a vertical plane due to the magnification of the image of one eye in the horizontal meridian

clues, not based on retinal disparities. The disparity factors form the foundation of binocular vision and true stereopsis. They result in the most exact *perception* of the relation of objects in space, the unocular clues allow an *interpretation* of the spatial relation of objects, but this interpretation is never as accurate as the actual perception afforded by the disparity factors.

It is important for the purpose of scientific analysis to emphasize the difference between these two sets of factors. But unerring orientation in space is made possible only by the constant interaction of both sets. The disparity factors are as such unchangeable, i. e., the simultaneous stimulation of the same two disparate retinal elements lying within fusional areas causes—in the absence of strong

3 Ogle, K. N. Analytical Treatment of the Longitudinal Horopter. Its Measurement and Application to Related Phenomena, Especially to the Relative Size and Shape of Ocular Images, *J. Optic. Soc. America* 22: 665, 1932, *Die mathematische Analyse des Längshoropters*, *Arch. f. d. ges. Physiol.* 239: 748, 1938.

unocular factors—the stimulating object point always to be localized in the same position in the subjective space of the observer. But the actual experience of the relation of objects in space is constantly modified and rectified by the unocular clues. If a condition exists in which the information conveyed by the disparity clues is in conflict with the information conveyed by the unocular clues, the latter may dominate if the field of vision contains a sufficient amount of perspective elements, such as are present in ordinary surroundings indoors. Also, the response to stereoscopic stimuli varies not only with different persons but with the same observer at different times. It depends on a number of circumstances whether the disparity factors or the unocular clues will prevail.

Every person with normal binocular vision experiences the distortional effect of meridional size lenses to the theoretically expected degree if his field of view contains a minimum of perspective elements. Such a field of view exists in natural surroundings, in the underbrush of a forest or on a lawn. It can be created artificially in laboratory experiments by using instruments in which the field of view is as devoid as possible of perspective and form factors. Such an instrument is, for instance, the apparatus by means of which the empiric horopter⁴ is determined. The curve of the longitudinal empiric horopter always undergoes a rotation about a vertical axis through the fixation point when a difference in the size of the ocular images is introduced in the horizontal meridian (fig. 2).⁵ This rotation is strictly proportional to the amount of magnification introduced and has been termed by Ogle “the geometric effect” of the size lenses on the longitudinal horopter, because the geometric explanation conforms so closely to the subjective spatial localization.⁶

It is known now what takes place when a normal person introduces in front of one eye a meridional size lens at axis 90. The problem which arises and which I have attempted to solve is this: What happens to the appearance of space and to an observer's functioning within space when a meridional size lens is worn constantly for a certain length of time? Do the spatial distortions of the normal surroundings remain unchanged? Does the rotation of the horopter curve remain the same? Does the capacity of compensating for artificially introduced meridional aniseikonic errors exist? And if compensation should occur, is it due to a physiologic change which reduces the artificially created disparity, or is it the result of a modification of the interpretation of the relation of objects in space due to an increasing effect of the unocular factors?

4 The horopter is defined as the locus in space of the object points imaged on corresponding retinal elements of the two eyes. If the corresponding retinal elements were distributed equally on the two sides of the fovea of each eye, the intersection of the visual plane with the surface of the horopter (the “longitudinal” horopter) would be the circle determined by the fixation point and the centers of the pupils of the two eyes (Vieth-Müller circle, fig. 2). Actually, such a regular distribution of the retinal elements—or rather of the spatial values of the retinal elements—does not occur, and the empiric longitudinal horopter differs, therefore, from the Vieth-Müller circle. This difference in shape has been termed the Hering-Hillebrand deviation of the curve of the empiric longitudinal horopter. For near vision fixation distance (40 to 75 cm) the longitudinal horopter curve is concave toward the observer and lies somewhere between the Vieth-Müller circle and the objective fronto-parallel plane (fig. 2). Owing to the discrepancies in the distribution of the spatial values of the retinal elements between the two eyes, the curve of the empiric longitudinal horopter is frequently not symmetric.

5 Ames, A., Jr., Ogle, K. N., and Gliddon, G. H. Corresponding Retinal Points, the Horopter and Size and Shape of Ocular Images, *J. Optic. Soc. America* **22** 619, 1932.

6 Ogle, K. N. Induced Size Effect: A New Phenomenon in Binocular Vision Associated with the Relative Sizes of the Images of the Two Eyes, *Arch. Ophth.* **20** 604 (Oct) 1938.

Answers to these questions would be of interest in themselves, since they might permit a direct insight into the interrelation of the disparity and unocular factors in the total act of space perception. They would also be of practical importance in offering an explanation as to how patients with aniseikonia deal with the problem of spatial orientation. Aniseikonia of clinically significant amount is frequent and always causes a measurable disturbance of spatial orientation.⁷ Yet complaints about difficulties arising from such a disturbance are rare, and persons with a clinically significant amount of aniseikonia seem to get around as well as persons with an insignificant amount. How can this apparent contradiction be explained?

Finally, experiments in which size lenses are worn for a period of time may shed some light on the validity of the contention that it is superfluous to correct aniseikonic errors, since many persons become accustomed to even larger differences in the size of the images of the two eyes than are currently equalized in clinical practice by means of iseikonic lenses.

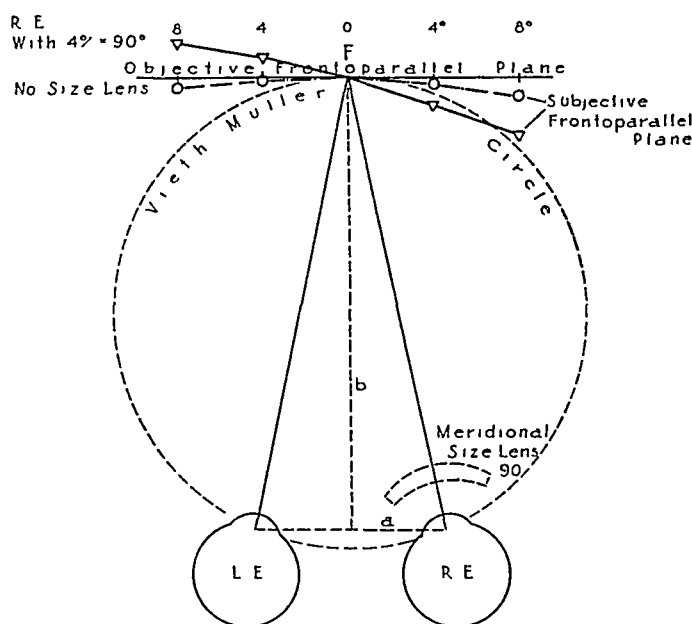


Fig 2—Rotation of the curve of the empiric longitudinal horopter (apparent frontoparallel plane) under the influence of a meridional size lens magnifying the horizontal meridian by 4 per cent (Data of M E B, fixation distance, 40 cm)

This paper reports results obtained by three observers who wore size lenses at axis 90 in front of one eye for a period of eight to ten days, during which time measurements were made two to three times a day with the horopter apparatus, the space eikonometer, the standard eikonometer and a rotating plane apparatus. These experiments showed that there was a complete adaptation in ordinary surroundings abundant in unocular factors to the spatial distortions introduced by the size lenses. However, in the instruments with a field of view containing a minimum of perspective factors, the presence of the greater part of the artificially introduced size difference could always be demonstrated.

INSTRUMENTATION AND EXPERIMENTAL PROCEDURE

A Instrumentation—The instruments used for the determination of the relative difference between the ocular images produced by the wearing of a meridional size lens in front of one eye

⁷ Ogle, K N Association Between Aniseikonia and Anomalous Binocular Space Perception, Arch Ophth 30 54 (July) 1943

were the horopter apparatus, the space eikonometer, the standard eikonometer and a rotating plane apparatus with perspective patterns

The curve of the longitudinal horopter can be determined most rapidly and conveniently by means of the criterion of frontoparallelism. This is achieved by having the observer fixate a vertical wire situated at a given distance in the median plane of his head and having him then set a number of vertical wires to the right and left of the fixation wire as seen in peripheral vision in such a way that all wires appear to him in a plane parallel to his forehead. This subjective or apparent frontoparallel plane is more or less at variance with the

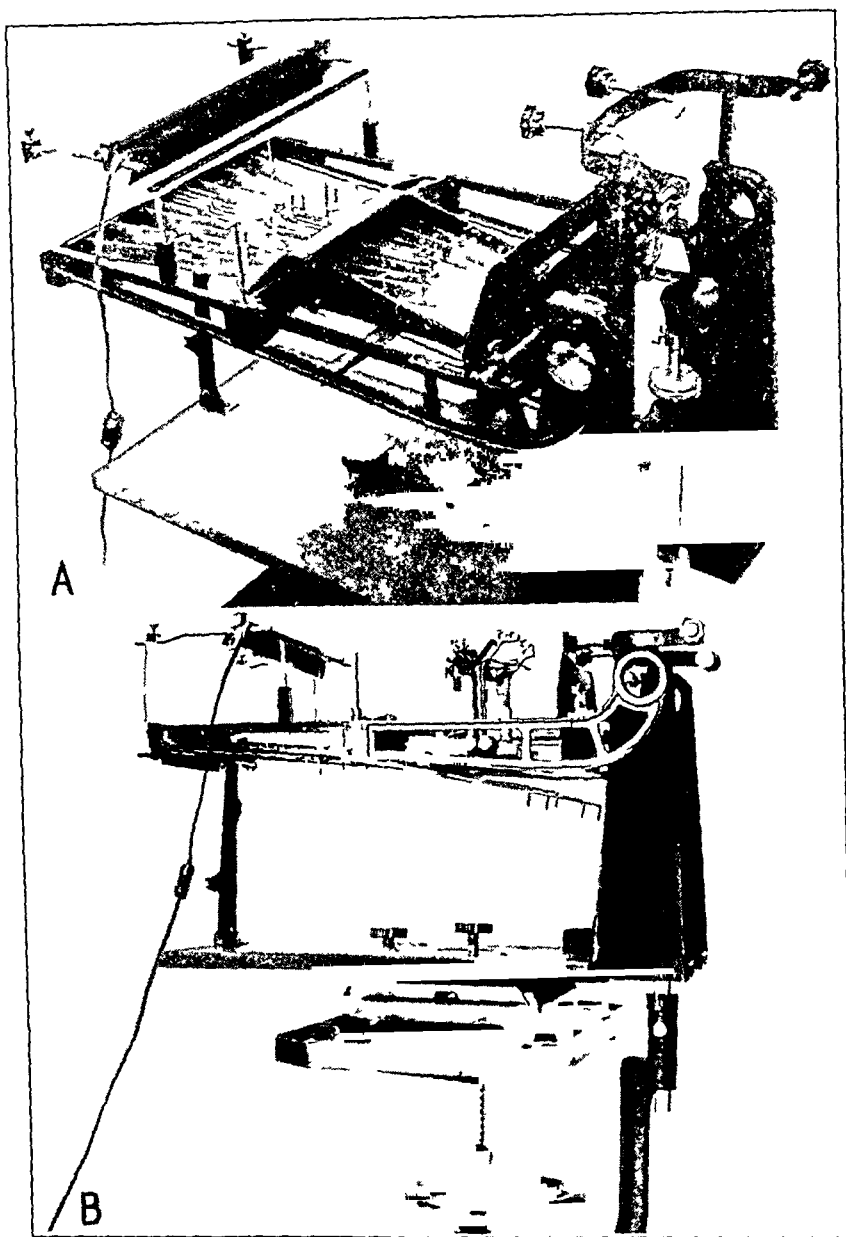


Fig 3—The horopter apparatus *A*, front view, *B*, side view

objective frontoparallel plane (fig 2), but the settings for the same observer are constant within very narrow limits of error

The particular horopter apparatus used in these experiments (fig 3) was a somewhat simplified instrument of the type described in detail by Ames, Ogle and Gliddon in their fundamental paper⁵. It consists of a number of metal channels, or lanes, which are so arranged as to converge toward a point situated under the midpoint of the basal line of the observer. In these channels metal strips can be moved by means of handles, and on these strips carriers are mounted which support vertical steel wires used as test elements in the determination of the apparent frontoparallel plane. The central wire is mounted at 40 cm from the midpoint of the observer's basal line and serves as the fixation wire, the other four wires are movable and are located in symmetric lanes at 4 and 8 degrees, respectively,

on each side of the fixation wire. Permanent records of the settings are obtained by means of small punches fastened to the supports of the vertical wires. If the criterion of the common visual directions is to be used for the determination of the horopter curve (nonius horopter) instead of the criterion of frontoparallelism, an attachment is used in front of the wires. This attachment has the form of an illuminated screen with special apertures which cause each of the peripheral wires to be seen in its upper half by one eye and in its lower half by the other eye. The movement back and forth of the wire in the lane causes an apparent sidewise movement in opposite directions of the two monocularly seen halves. The setting is completed when the two halves seem to form a continuous vertical line, since they are then presumably imaged on corresponding vertical sections of the retinas.⁸

The space eikonometer, an instrument recently developed by A. Ames Jr., which was also used in the experiments, has been described by Ogle,⁷ and the standard eikonometer and its use have been repeatedly discussed,⁹ it is, therefore, sufficient to mention that these instruments were used and to refer to the publications for their description.

The rotating plane instrument with perspective patterns (fig. 4) consisted essentially of white matte cardboard sheets with various patterns (lines, rectangles, circles, ovals, etc.) any one of which could be mounted on a suitable base for rotation about a vertical axis of symmetry. The cardboard could be rotated by means of two metal rods projecting from the sheet carrier toward the observer and extending beyond the aperture through which the observer looked at the patterns. The head of the observer was so adjusted in a head rest that its median plane coincided with a plane through the center of the cardboard and normal

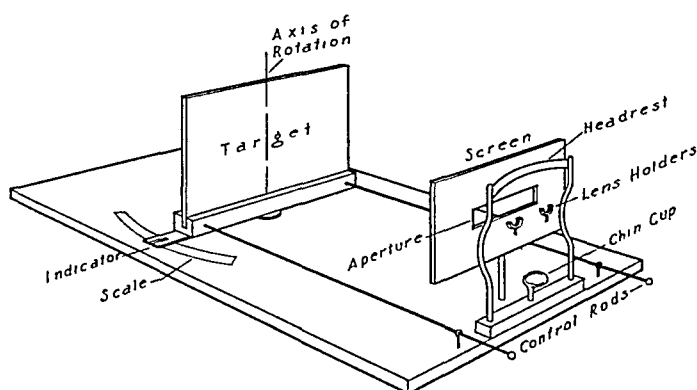


Fig. 4.—Diagrammatic representation of the frontal plane instrument with perspective patterns

to the objective frontoparallel plane of the instrument. A septum in this median plane prevented the binocular view of extraneous objects. Adjustable cells in front of the observer's eyes allowed the insertion of size lenses or other auxiliary lenses. The center of the cardboard was at 40 cm from the midpoint of the basal line of the observer, and the cardboard was lighted in such a way that the illumination remained unchanged when the cardboard was rotated. A degree scale and indicator at the end of the sheet carrier permitted an assistant to read the angle between the cardboard and the objective frontoparallel plane of the instrument. The task of the observer was to set the cardboard in a plane which appeared to him to be parallel to his forehead; there were no restrictions as to the fixation of his gaze.

B Experimental Procedure—The procedure followed in the experiments was simple. For a number of days, usually from four to seven, preliminary measurements were taken the first thing in the morning and late in the afternoon to establish the observer's normal condition. Immediately before and after addition of the size lens, measurements were taken,

⁸ The data obtained with both types of settings of the horopter apparatus were treated in the way described by Ogle.³ The actual data (the "spatial curves" of the longitudinal horopter) were transformed into analytic graphs indicating the image size difference present and the slope of the horopter curve.

⁹ Carleton, E. H., and Madigan, L. F. Size and Shape of Ocular Images. II. Clinical Significance. *Arch. Ophth.* 7:720 (March) 1932. Ogle, K. N., and others. Repeatability of Ophthalmo-Eikonometer Measurements, *ibid.* 24:1179 (Dec.) 1940. Burian, H. M. Clinical Significance of Aniseikonia, *ibid.* 29:116 (Jan.) 1942.

and while the size lens was worn the same routine was followed as in the days preceding the experiment proper. One of the observers also regularly took measurements late at night. The size lens was worn for eight to fourteen days, and the observers were never for a single waking moment without it. If the spectacles had to be removed, one eye was always closed until they were again put on, in the morning before the first measurement was taken one eye was as a rule occluded. The observers were requested to keep a diary as to their activities and experiences while wearing the lens. Immediately before and after removal of the lens, measurements were again taken and the routine continued until the observer showed normal readings. This took from four to ten days, so that the three stages of each experiment were completed in from three to four weeks.

The experiments reported were made by three nonpresbyopic observers, all of whom had normal corrected visual acuity and normal binocular vision. One of them is a myope, the other a hyperope and the third an emmetrope. The emmetrope was not accustomed to the wearing of glasses, and in the preliminary stage of the experiment plano spectacles were used to which the size lens was later attached.

EXPERIMENTAL RESULTS AND COMMENT

A *The Effect of Wearing a Meridional Size Lens*—All experiments gave in general the same result. When the size lens was first added the familiar surroundings took on an unusual appearance, showing the typical spatial distortion introduced by a meridional size lens worn at axis 90. This distortion was more marked in near vision than at distance, it was more pronounced when attention was paid to the shape of things and when the observer fixated an object point instead of letting his glance rove. With continued wearing of the lens, the distortion gradually subsided and finally disappeared. During the last few days the lens was worn it was usually impossible for the observer to detect the distortion in familiar surroundings even when he was giving close attention to the position and shape of objects. The time necessary to become accustomed to the lens varied with the strength of the lens but was never longer than three or four days.

It must be noted that the wearing of the lens caused some definite discomfort. Slight headaches and eyestrain were general, as was a feeling of irritability and nervous tension. I regularly had some gastric distress. The 3 observers did not all have symptoms of the same degree, but none could wear the lens without some unpleasant effect. There was pronounced relief when the lens was eventually removed, although the intensity of all symptoms decreased the longer it was worn.

On the whole, all the observers could go about their duties without great inconvenience, the distortions did not interfere materially with the finer tasks of visuomanual coordination, but I felt that I had to avoid the performance of such operative procedures as cataract extractions during the first days I wore the lens.

As far as the ordinary urban surroundings were concerned, the adaptation to the artificially introduced size difference seemed complete. However, when one went out into the fields or onto a hill with high-grown autumn grass, or in general into surroundings with but few rectilinear, perspective factors, the distortion returned immediately. This happened time and again, it happened even on the very last day the lens was worn. This phenomenon is an established fact.

These observations suggest that one is able to become accustomed to artificially introduced image size differences in the sense that objects are seen in their true shape and localized correctly in space as long as there are in the field of view perspective clues in sufficient number and of sufficient intensity to dominate the stereoscopic factors and to permit a reinterpretation of space. But when there are only few and scanty perspective clues in the field of view, the stereoscopic factors become again effective and the distortion recurs.

B *Quantitative Results with the Horopter Apparatus*—The information obtained from the quantitative determination of the image size difference during the experiments must now be considered

The curve of the empiric horopter as determined by the criterion of fronto-parallelism showed that the initial rotational effect produced by the size lens diminished gradually, at first fast and then more slowly, until finally a certain level was reached, beyond which no further decrease in the effectiveness of the lens occurred. As an example, the curve obtained in one experiment is reproduced in figure 5. However, the effectiveness of the lens was never completely lost, the decrease ranged on the average from one fifth to two thirds of the initial effect. The results obtained with the horopter instrument in 10 experiments are summarized in table 1. The first column records the size lens used, the second the initials of the observer, the third the eye in front of which the lens was worn and the fourth the number of days during which the lens was worn. Then follows the immediate effect of addition of the size lens in terms of percentage size difference

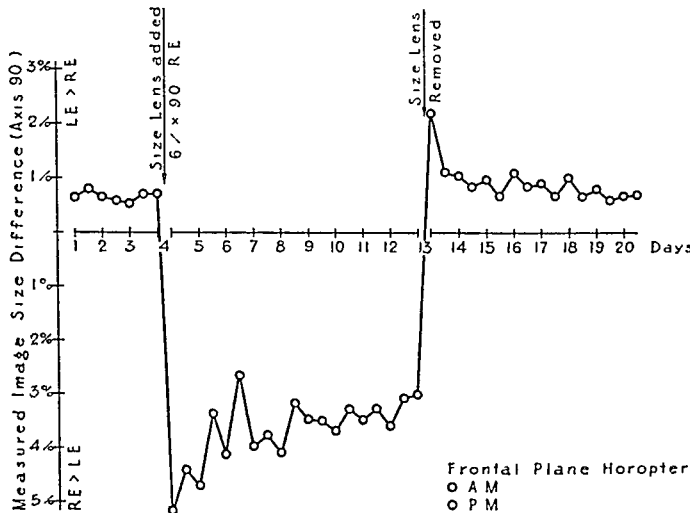


Fig 5—Diagram representing the differences in the size of the images of the two eyes as determined by the criterion of the apparent frontal plane in an experiment in which the observer (R E B) wore a meridional size lens of 6 per cent at axis 90 degrees in front of the right eye

between the ocular images, and the average decrease in the effectiveness of the lens measured during the last two or three days the lens was worn. In the next column this decrease is expressed in percentage of the initial effect of the size lens. The eighth and ninth columns contain the maximum decrease in a single setting and its amount in percentage of the initial immediate effect of the lens. The tenth column records the effect in percentage size differences measured immediately after the removal of the lens

This table reveals a number of interesting results. It shows, first of all, that the amount of average and maximum decrease in the effectiveness for different size lenses differs for different observers. But it also shows that the decrease differs with the eye in front of which the lens is worn. Thus, the effect of a size lens of 3 per cent worn by the two observers H M B and R E B in front of the right eye was reduced by about 50 per cent at the end of the experiment, whereas when the lens was worn in front of the left eye the decrease in effectiveness was only about 20 per cent

This result cannot be fully explained at this time, but it is undoubtedly worthy of further attention. All that can be said is that there is a marked discrepancy in the residual amount of size difference produced by the prolonged wearing of size lenses according to whether the image of the right or the left eye is magnified in the horizontal meridian. Experience has shown that numerous persons when tested at the tilting field¹⁰ or in the leaf room⁷ do not respond equally well when size lenses are placed in front of the right and the left eye, respectively. This fact may have some bearing on the problem under consideration, but it cannot explain it, since the 3 observers reacted equally well to size lenses put in front of either eye (fig. 6). It may, however, be assumed that it is possibly easier to overcome the disparity factors and reinterpret the position of objects in space according to the unocular factors if the image of one eye rather than that of the other is magnified. This may conceivably be connected with the ocular dominance of the subject, and it is to be expected that further research will uncover a relationship between ocular

TABLE 1—*Average and Maximum Decrease in Effectiveness of Meridional Size Lenses Worn at Axis 90 Degrees in Front of One Eye for a Number of Days as Determined by the Apparent Frontal Plane Horopter Curve*

Size Lens (%)	Observer	Eye Before Which Lens Was Worn	Time During Which Lens Was Worn (Days)	Immediate Effect When Lens Was Added (%)	Average Decrease of Effective-ness of Lens in Percentage Size Difference	Average Decrease of Effective-ness in Percentage of Immediate Effect	Maximum Decrease of Effective-ness of Lens in Percentage Size Difference	Maximum Decrease of Effective-ness of Lens in Percentage of Immediate Effect	Immediate Effect After Removal of Lens
6	H M B	Right	8	5.63	2.51	45	3.79	66	6.69
	R E B	Right	8	5.85	1.83	32	2.18	37	5.10
3	H M B	Right	8	2.44	1.73	70	2.10	86	2.57
	H M B	Right (repeat)	15	2.45	1.02	42	1.49	61	2.99
	H M B	Left	10	2.94	0.55	19	0.81	28	2.79
	R E B	Right	8	2.87	1.45	51	1.78	62	2.60
	R E B	Left	9	2.63	0.59	22	1.02	39	2.86
	M E B*	Right	8	2.76	0.40	15	0.61	22	2.42
	M E B	Right	13	2.54	0.62	24	0.89	35	2.26
1.5	H M B	Right	11	1.30	0.83	64	1.33	100	1.62

* These data were taken with a somewhat different setup of the horopter instrument.

dominance and the response to disparity and perspective factors. But this more intricate question cannot be answered until one knows more about the way in which the adaptation to artificially created size differences takes place.

Since the spatial distortion due to meridional size lenses worn at axis 90 tends to disappear entirely in surroundings offering numerous perspective clues, it was first concluded that the longer the lenses are worn the more the subject learns how to disregard the disparity factors and to reinterpret the surroundings on the basis of the unocular factors contained in them. The adaptation to the artificially introduced size differences would accordingly be due to a psychologic reinterpretation, not to a physiologic compensation. This explanation, however, does not seem to be borne out by the quantitative experiments. If it were correct, one would not be able to find any compensation in the measurements with the apparent frontal plane horopter, the space eikonometer or the standard eikonometer, since perspective factors are excluded as far as possible from the field of view of these instruments. Yet, as has been shown, there is evidence, even with these instru-

¹⁰ Ames, A., Jr. Aniseikonia: A Factor in the Functioning of Vision, *Am J Ophth* 18:1014 (Nov.) 1935.

ments, of a decrease in the effectiveness of the size lenses of from one fifth to two thirds of the initial effect. This would argue in favor of a true physiologic compensatory process, a tipping of the crystalline lens or the like, which would partially offset the artificially introduced size difference.

In trying to understand the nature of the compensation which is apparent in the measurements, one must keep in mind that the adaptation is complete in ordinary surroundings and that the lack of unocular factors must play some part in this adaptation, since the distortion recurs immediately when there are only a few perspective factors. On the other hand, the perspective factors, although reduced to a minimum, are not entirely excluded in the instruments used. The reinterpretation of spatial relationships which the observer is forced to make while wearing the lenses creates memory values which might well mold to a certain extent the interpretation given to the disparity clues. It stands to reason that an observer who is incessantly exposed to an overwhelming number of unocular factors in his surroundings will not be able to free himself entirely from their influence during the ten or fifteen minutes which it takes to make the measurements. One can therefore, assume that the partial compensation evident in the

TABLE 2—*Difference Between the Settings of the Apparent Frontoparallel Plane in the Morning and in the Evening While Size Lenses Were Worn*

Observer, Eye, Lens	Average Decrease of Effectiveness of Lens in Percentage Size Difference	Average of Morning Settings While Lens Was Worn (%)	Average of Evening Settings While Lens Was Worn (%)	Difference Between Morning and Evening Settings (%)
H M B right, 6% axis 90	2.51	Right 3.85	Right 2.26	1.59
R E B left, 3%, axis 90	0.59	Left 2.39 (Left 2.68)*	Left 1.75 (Left 1.61)*	0.66 (1.07)*

* The figures in parentheses indicate the average settings and their difference during the first five days of the experiment, during which an occluder was worn in the morning.

measurements with the various instruments is due to the influence of memory values created by the unocular factors.

There is no actual proof for the correctness of this assumption, but there are some results which seem to support it. One of them is the fact—which has been confirmed by all experiments performed by the 3 observers—that the decrease in effectiveness of the size lens as measured with the three instruments is smallest in the morning and greatest at night. This phenomenon is in itself of considerable interest. It indicates that the essential physiologic binocular cooperation afforded by the disparity factors is more prevalent after sleep, which has to some extent wiped out the memory values created by the unocular factors. And this, incidentally, throws some light on the essence of sleep as a recuperative process. The difference between the measurements taken in the morning and those taken at night is even more marked when an occluder is worn over one eye from the moment the subject arises until the first measurements are taken. This finding may be of some clinical importance, it suggests that occlusion should be tried in cases in which there is a suspicion that measurements with instruments such as the standard eikonometer do not reveal the full error. But whether or not an occluder is worn, toward the end of the experiments the differences between morning and evening settings level off more and more. Table 2 shows the average of the morning and evening settings in 2 experiments.

The difference between the morning and evening settings could, of course, also be explained by a reversible process of actual physiologic compensation, which

would have to be set in action every morning by binocular stimulation. But there is another observation which strongly supports the interpretation theory. While a size lens is worn the first of the five settings of the horopter wires, the average of which constitutes one reading of the apparent frontal plane horopter, frequently shows a greater compensation than the last one. The five apparent frontal plane horopter settings usually do not take more than five to seven minutes, and the differences between the first and last settings can, therefore, not be very pronounced. The measurements on the standard eikonometer and the space eikonometer require as a rule a longer time, and it is significant that the longer the observer looks into the space eikonometer or at the standard eikonometer pattern, the more will the artificially introduced size difference become manifest. Thus, in the case of observer R. E. B., who was wearing a meridional size lens of 3 per cent over the right eye, a quick check with the standard eikonometer and the space eikonometer revealed in the afternoon of the third day of the experiment that the image seen by the right eye was larger by 2 per cent. But after the observer looked into either instrument for about one-half hour the manifest size difference increased to 2.75 per cent for the right eye. Since the observer during all this time was subject to binocular stimulation, it would seem that the increase in the effectiveness of the lens could be attributed only to the fact that the longer an observer watches a field which is relatively free from perspective factors, the more he frees himself of the memory values of the previous experiences and the more he is apt to give weight to the disparity factors.

Another diurnal change warrants a brief mention. When measurements were taken at night, the manifest size difference was frequently larger than in the afternoon. This is apparently a phenomenon of fatigue and would indicate that the unocular factors are less effective in a fatigued observer than in an unfatigued one. The phenomenon was more apt to occur when the observer had worn a size lens for a number of days, but it did not take place with regularity. Such a regularity would not be expected, since fatigue is not a constant factor. Only one observer (H. M. B.) has more or less regularly determined the horopter curve in the evening hours, and these deductions apply only to his data, but these are quite convincing, as can be seen from the examples in table 3.

There is another factor which one should consider in trying to understand the nature of the adaptation to meridional size lenses. The settings of the apparent frontoparallel plane, based on the disparity factors, show a high degree of accuracy, in fact, the empiric longitudinal horopter has been defined as the locus of maximum stereoscopic sensitivity.¹¹ Interpretative judgments in spatial localization have a much lower degree of accuracy. One might, therefore, argue that in the case of a physiologic change the mean deviations should not differ essentially, whether or not a lens is worn, a decrease in accuracy would be in favor of an interpretative process. Table 4 shows the average of the mean deviations in millimeters of the spatial longitudinal horopter curves. It can be seen from the figures that the average mean deviations are higher while size lenses are worn by 0.2 mm for the outer wires and by 0.1 mm for the inner wires, this fact indicating that the settings are less precise under those circumstances. Since the mean deviations for the outer wires when no size lens is worn are roughly double those for the inner wires, the accuracy of the settings is impaired proportionally over the whole field by about one third. This increase in the mean deviations may be attributable in part to the

11 Tschermak, A. Optischer Raumsinn, in Bethe, A., and von Bergmann, G. Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1931, vol. 12, pt. 2, p. 899.

fact mentioned that the first in a group of five settings often shows a smaller size difference than does the last one when size lenses are worn

Not only the accuracy of the settings but the response to additional size differences might be affected by a process of compensation for artificially introduced

TABLE 3—*Examples of Diurnal Changes in the Manifest Size Difference as Determined by the Rotation of the Apparent Frontal Plane Horopter When a Meridional Size Was Worn in Front of One Eye (Observer H M B)*

Size Lens Worn	Day of Experiment	Hour	Size Difference Measured (Right Eye, %)
6%, axis 90°, right eye	First	9 15 a m	5 00
		1 15 p m	2 74
		11 15 p m	2 40
	Third	8 45 a m	3 48
		2 15 p m	2 52
		10 15 p m	2 84
	Sixth	9 00 a m	3 52
		2 00 p m	2 00
		7 15 p m	2 45
3%, axis 90°, right eye	First	8 30 a m	2 28
		4 00 p m	1 54
		10 00 p m	1 12
	Fourth	9 00 a m	1 30
		4 00 p m	1 05
		10 00 p m	1 30
	Seventh	11 00 a m	0 84
		6 00 p m	1 25
3%, axis 90°, right eye	Second	9 45 a m	2 15
		2 30 p m	1 57
		6 30 p m	1 35
	Third	9 55 a m	2 04
		2 30 p m	1 25
		11 15 p m	1 52
	Fourth	10 00 a m	1 85
		4 15 p m	1 59
		10 15 p m	1 54
	Eighth	8 30 a m	1 26
		1 40 p m	1 23
		9 20 p m	1 44

TABLE 4—*Summary of Mean Deviations for Experiments Recorded in Table 1*

Observer	Condition	Number of Settings	Lane			
			—8	—4	+4	+8
H M B	Before lens was worn	155	0 60 ± 0 10	0 28 ± 0 03	0 28 ± 0 06	0 34 ± 0 03
	While lens was worn	545	0 79 ± 0 09	0 39 ± 0 03	0 40 ± 0 06	0 74 ± 0 15
	After lens was worn	340	0 61 ± 0 06	0 31 ± 0 04	0 33 ± 0 01	0 63 ± 0 06
R E B	Before lens was worn	125	0 47 ± 0 11	0 26 ± 0 04	0 31 ± 0 06	0 58 ± 0 03
	While lens was worn	365	0 68 ± 0 10	0 37 ± 0 01	0 41 ± 0 06	0 79 ± 0 13
	After lens was worn	200	0 40 ± 0 05	0 22 ± 0 05	0 26 ± 0 06	0 43 ± 0 04
M I B	Before lens was worn	75	0 49 ± 0 08	0 22 ± 0 00	0 23 ± 0 03	0 50 ± 0 10
	While lens was worn	105	0 69 ± 0 10	0 32 ± 0 01	0 25 ± 0 01	0 51 ± 0 09
	After lens was worn	110	0 49 ± 0 05	0 26 ± 0 01	0 29 ± 0 04	0 54 ± 0 04

size differences This possibility was checked in every experiment, but all observers showed the same geometric effect before, while and after the lens was worn except that the zero position was shifted according to the residual effect of the size lens In other words, their sensitivity to disparate stimulations as determined by their response to artificial meridional image size differences of from 1 to 4 per cent was not impaired by their wearing a meridional size lens, as can be seen from figure 6

The slopes¹² were determined for all horopter curves taken during the experiments. There is a tendency for the curves to be steeper when size lenses are worn, in all but 2 of the experiments reported in table 1 the average slope was higher during the experiment than before and after. The average increase of the slopes for all experiments of observer H M B was 0.11 and for those of observer R E B 0.15; for observer M E B the average increase was zero. The increase would indicate a change in shape of the horopter curve in the direction of less concavity (increase in the Hering-Hillebrand deviation, the curve tends to approach the objective frontoparallel plane) under the influence of prolonged wearing of meridional size lenses, but this is a trend rather than a definite occurrence.

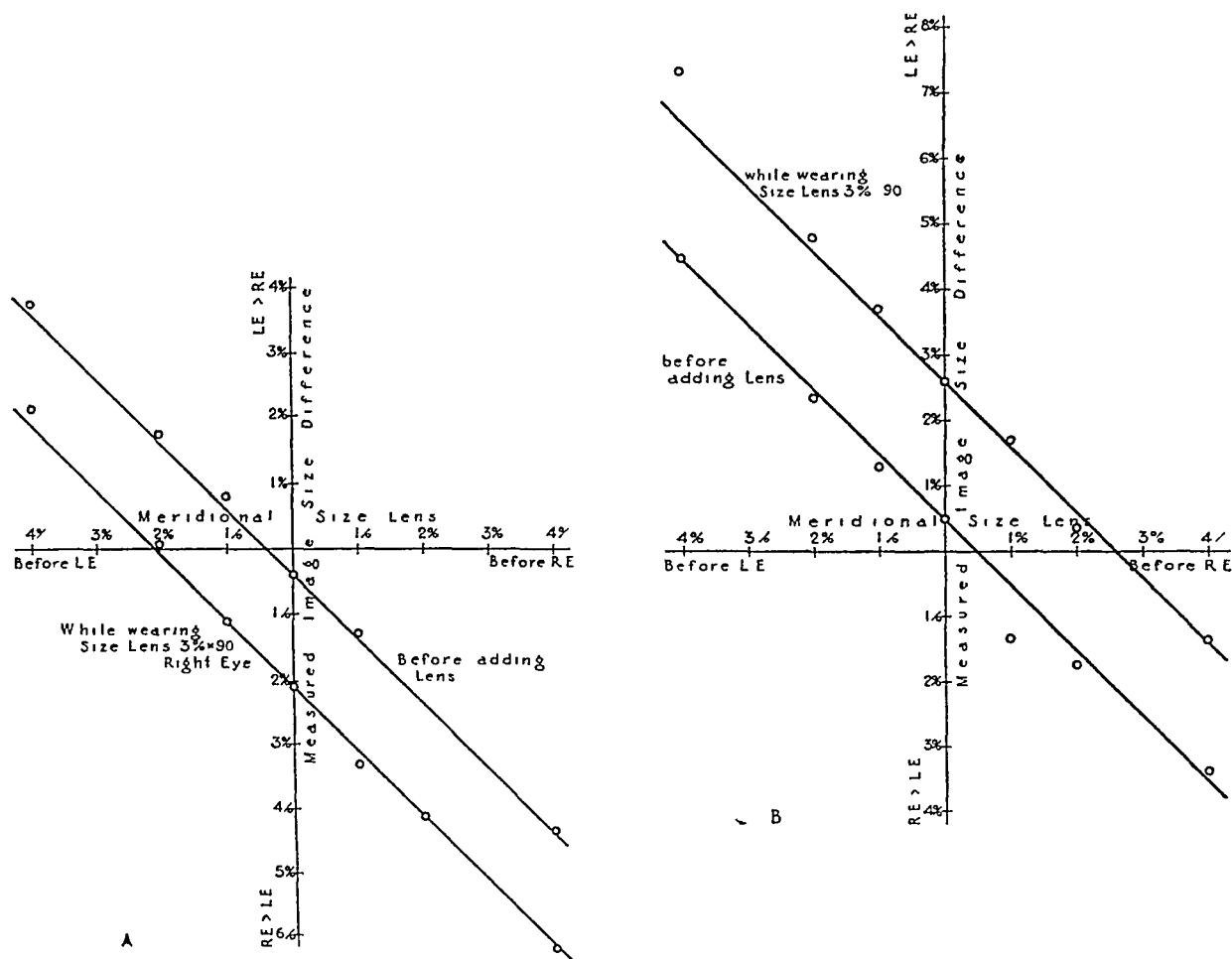


Fig 6—Sensitivity to meridional size lenses placed in front of each eye before and while a size lens was worn. The abscissa indicates the lens placed in front of the eyes, the ordinate, the response (the resulting image size difference) as determined by the criterion of the apparent frontoparallel plane. A, data of observer M E B, B, data of observer R E B.

While the setting of the apparent frontoparallel plane by means of the wires of the horopter apparatus is to a certain extent subject to the influence of perspective factors, any direct influence of these factors is excluded when the nonius horopter is used. This is due to the fact that an entirely different criterion is used and that the settings are independent of the position of the wires relative to each other.

¹² The slope of the horopter curve, derived from the analytic transformation of the spatial curve, is a measure of the deviation of the entire horopter curve from the Vieth-Müller circle and, therefore, a measure for the Hering-Hillebrand deviation of the horopter curve.⁴ When the slope is zero, the horopter curve coincides with the Vieth-Müller circle, when positive it deviates in the direction of the objective frontoparallel plane.

and to the fixation wire. The behavior of the nonius horopter would be, therefore, of some importance with regard to the question under discussion. However, the nonius horopter settings are extremely difficult and are vitiated by certain other factors. So far only 1 of the observers (H. M. B.) has made preliminary studies with this method, and these have shown that for him in general the nonius horopter readings indicate a much larger image size difference than the readings with the apparent frontal plane method and, furthermore, that by this method no loss of effectiveness seems to be apparent when a meridional size lens is worn. The first fact if borne out by further studies would imply that this method permits one to determine the full size difference present, which is otherwise partly masked, the second, that there is actually no compensation for an artificially introduced size difference and that the apparent compensation is due to other than physiologic factors. Further investigations along these lines are necessary.

C Quantitative Results with the Space and Standard Eikonometers—The measurements with the horopter instrument give information only about size dif-

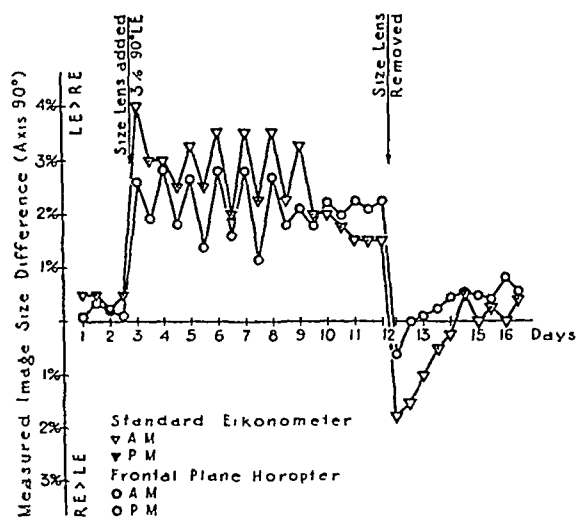


Fig 7—Diagram representing the differences in the size of the images of the two eyes as determined by the standard eikonometer (near vision, axis 90 degrees) and the horopter apparatus in an experiment in which the observer (R. E. B.) wore a meridional size lens of 3 per cent at axis 90 degrees in front of the left eye.

ferences in the horizontal meridian. There is the possibility that during the time the lenses are worn some changes might occur in the vertical and oblique meridians which would explain the reduced effectiveness in the horizontal meridian. In order to investigate this possibility measurements were made with the space eikonometer and the standard eikonometer.

These measurements showed that there was no change whatever in the vertical and oblique meridians, the measurements remained the same throughout the experiment. No transformation of the horizontal into vertical or oblique size differences took place, but a decrease in the effectiveness of the size lens was found similar to that with the horopter apparatus. Figure 7 shows an example of the curves resulting from 1 experiment.

A comparison of the results obtained with the various instruments is of interest. Some of these results are summarized in table 5. As can be seen from these data, the trend is the same with all three instruments. If anything the

measured decrease in the response to the size lens in the horizontal meridian was higher with the space and standard eikonometers, especially for observer R E B.

In view of the different bases of the three methods it was of interest to correlate the measurements obtained with the three instruments. While one is making horopter settings, fixation is strictly maintained, in the space eikonometer a similar criterion as in the horopter instrument is used, but the observer's gaze is not fixed, in the standard eikonometer the observer has to move his eyes 4 degrees from the fixation point up, down and sideways, and an altogether different criterion is used in the determination of the image size difference. The data obtained in all experiments were correlated, but I shall report here as an example only the figures for the data of observer R E B, for which the scatter diagrams are given in figure 8. The Pearson correlation coefficient was high when all data were taken into account, the horopter and space eikonometer measurements at axis 90 correlated by 0.92, and the horopter and the standard eikonometer measurements at axis 90 by 0.98.

TABLE 5—*Comparison of Results Obtained in 3 Experiments with the Apparent Frontal Plane Horopter, the Space Eikonometer and the Standard Eikonometer*

Observer, Eye, Lens	Instrument	Immediate Effect of Addition of Size Lens (%)	Average Decrease in Effective- ness of Size Lens in Percentage Size Difference	Average Decrease in Effective- ness of Size Lens in Percentage of Immediate Effect (%)	Lowest Single Reading While Lens Was Worn in Percentage Size Difference	Maximum Decrease in Effec- tiveness of Size Lens in Percentage of Immediate Effect	Immediate Effect After Removal of Size Lens
H M B 3%, axis 90°, right eye	Horopter	2.45	1.02	42	1.49	61	2.99
	Space eikonometer, axis 90°	2.94	1.37	47	2.10	71	3.16
M E B, 3%, axis 90°, right eye	Horopter	2.54	0.62	24	0.89	35	2.26
	Space eikonometer, axis 90°	3.07	0.61	20	0.74	24	2.47
R E B, 3%, axis 90°, left eye	Horopter	2.63	0.59	23	1.26	48	2.86
	Space eikonometer, axis 90°	2.88	1.08	38	1.35	47	2.87
	Standard eikonometer, axis 90°	3.25	1.50	46	2.25	69	3.75

However, when the data obtained while lenses were worn and after they were removed were considered separately, the picture was somewhat different. The correlation coefficient for the horopter measurements and the standard eikonometer measurements at distant vision was 0.80 after the removal of a 6 per cent size lens and 0.93 after the removal of a 3 per cent size lens. The data obtained while these lenses were worn showed a poor correlation, viz., 0.53 and 0.49, respectively. The generally high correlation of the measurements with the three instruments is further proof that all three measure the same thing—the difference in the size of the images of the two eyes. The low correlation of the measurements when lenses are worn can be considered as supporting evidence that the partial loss of effectiveness of the size lenses evident in the measurements is due to psychologic factors.

D *Quantitative Results with the Rotating Plane Instrument*—Instead of keeping the field of view of the observer as free as possible from perspective factors, one may deliberately add such factors to the field in order to determine their effect on the measurements. This would be an attempt to reproduce to a certain controlled extent the natural conditions of seeing and at the same time make a quantitative determination possible. To achieve this, the rotating plane instrument was used. The patterns employed were (a) five vertical lines the ends of which were seen by

the observer, (b) five vertical lines connected by a horizontal line at the top and at the bottom, (c) a large rectangle and (d) a large oval

The settings with this method proved to be both difficult to make and difficult to interpret. Instead of appearing to rotate, or while appearing to rotate, the pattern frequently changed its shape and the observer was induced to set the cardboard not according to the criterion of frontoparallelism but according to the shape of the

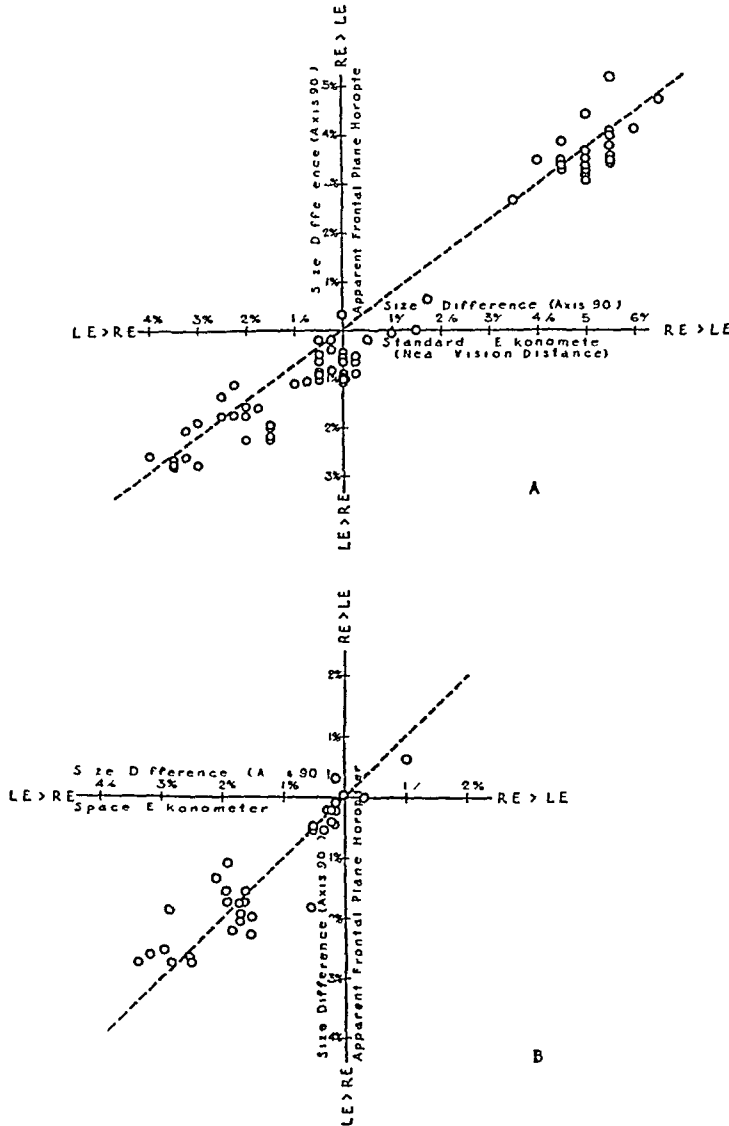


Fig 8—A, scatter diagram showing correlation of data obtained with the horopter apparatus and the standard eikonometer (near vision, axis 90 degrees) Data of R E B

B, scatter diagram showing correlation of data obtained with the horopter apparatus and the space eikonometer (axis 90 degrees) Data of R E B

elements of the pattern. The observer could never be quite sure that he was setting the cardboard consistently according to one or the other criterion, especially since the cardboard (the background) appeared sometimes to be in a plane different from the pattern itself. Theoretically, the arrangement raised a number of questions, such as the influence of form on frontoparallel settings, which are outside the scope of this paper. The results will, therefore, be reported only in so far as they have a bearing on the problem under discussion.

Preliminary experiments showed that there is a remarkable individual difference in the response to size lenses when patterns containing perspective elements are used as test objects. Some observers show little if any rotation, others respond more or less fully to the size lenses (figs 9 and 10). The explanation for this is that some persons give more weight to the disparity factors, while the visual act of others is dominated by the unocular factors. It might actually be

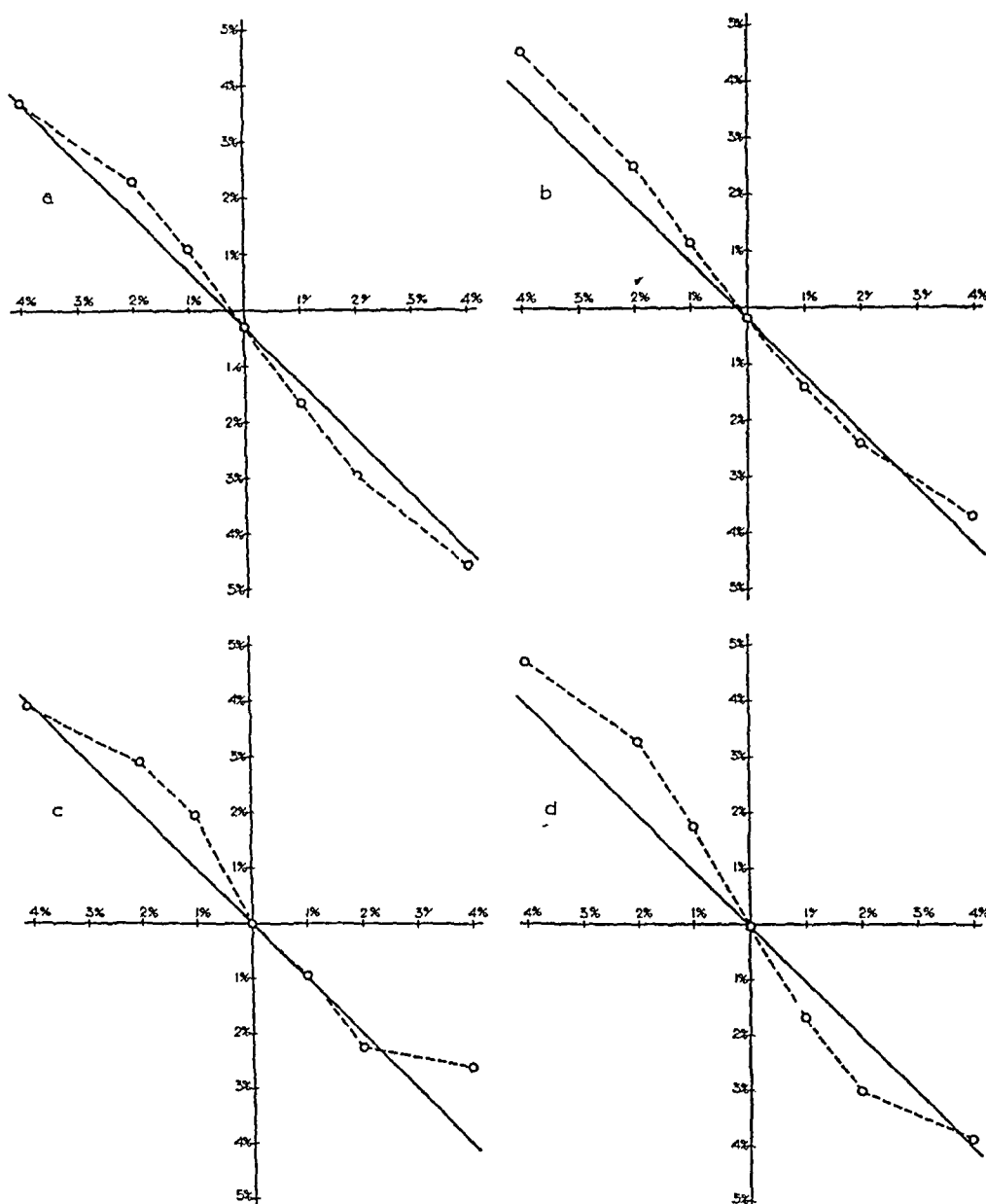


Fig 9—Response to artificially introduced size differences when perspective patterns were used. The abscissa indicates the size lens placed in front of the right eye (right half) or left eye (left half), the ordinate indicates the observer's response as determined by the rotation of the plane of the pattern. The patterns used were five vertical lines the end of which were seen by the observer (a), five vertical lines connected by a horizontal line at the top and at the bottom, (b), a large rectangle (c) and a large oval (d). This observer (M E B) showed a satisfactory sensitivity to meridional size lenses for most patterns.

possible to establish on this basis a typology of visual characters, and the result is, therefore, of broad general significance. Among the observers who wore size lenses the two extremes are represented by R E B, who showed little or no response to the size lenses when the patterns were used, and M E B, who responded as a

rule quite fully. The latter observer had the least tendency to show a decrease in the effectiveness of the size lenses, and it is possible that there is a causal relation between these two facts. It must also be mentioned that the different observers not only demonstrated individual differences in their sensitivity to size lenses when patterns were used but reacted differently at different times.

As to the result of the measurements with the rotating plane apparatus while size lenses were worn, observer R. E. B., who did not respond in the test with the perspective patterns consequently did not show any appreciable change in the measurements, while observer M. E. B., who responded more or less fully to size lenses with the patterns, showed a decrease in the effectiveness of the size lenses

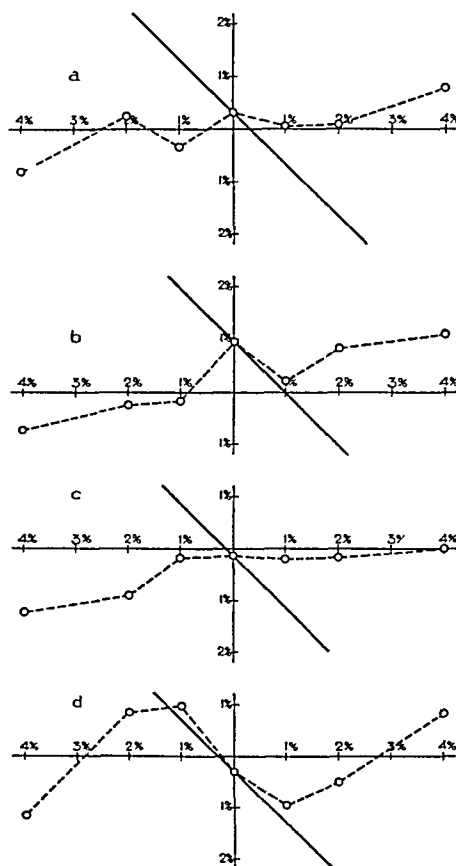


Fig 10—Response to artificially introduced size differences when perspective patterns were used. The significance of the abscissa and ordinate is the same as in figure 9, as are the patterns (a, b, c and d). This observer (R. E. B.) showed no response to meridional size lenses with any of the patterns.

worn which was about one-third greater than in the measurements with the horopter instrument.

E. Effect of Removal of Size Lens—The last experimental result which must be discussed is the effect produced by the removal of the size lens. As soon as the lens is removed, a considerable tilting of objects in space is noted *in the direction opposite to the one which occurs when the lens is first added*. In other words, the removal of the size lens from the right eye if the lens has been worn for some time acts as if a meridional size lens at axis 90 had been added to the left eye. This distortion not only is noticeable in the normal environment but is evident in a rotation of the horopter curve and in the measurements with the space eikonometer.

and standard eikonometer. The return to the normal condition is comparable to the process which takes place when the observer becomes accustomed to the added size lens. The effect lingers for some time—for from one to three days—in the usual surroundings and is again more marked in an environment lacking in unocular factors, but it decreases more rapidly than when a size lens is added and worn. However, in the measurements with the various instruments a residual effect can often be demonstrated a week or ten days after the removal of the lens.

It is again impossible to tell with certainty whether the process which takes place after the removal of the lens is due to a physiologic change or to a psychologic reinterpretation, but it is evident that the wearing of a meridional size lens creates a new equilibrium which is not immediately replaced by the normal equilibrium. The normal condition has to be reacquired by a process similar to the one which created the equilibrium when the lens was worn.

CONCLUSIONS

The evidence presented in the foregoing pages can be summarized as follows.

When a person with normal binocular vision places a meridional size lens at axis 90 in front of one eye and wears this lens for several days, he at first experiences a typical distortion of his surroundings. The longer the lens is worn, the less the distortion is noticeable, and it finally disappears and is absent as long as the observer remains within surroundings abundant in perspective and other unocular elements. There is, apparently, a complete adaptation to the distortion created by the lens in normal surroundings.

However, if the number of effective perspective factors in the surroundings is negligible, the distortion recurs immediately, and measurements made with instruments from whose field of view these factors are absent show that the larger part of the image size difference is still present, no matter how long the size lens is worn. But there is an average decrease in the effectiveness of the size lens of from one fifth to two thirds as measured with these instruments. This decrease in effectiveness could be due either to a process of actual physiologic compensation, leading to a redistribution of the stimuli on the retinas, or to a psychologic reinterpretation of the relation of objects in space under the influence of unocular clues in the surroundings and of memory values of past experience. There is no conclusive proof for either theory, but the weight of the evidence seems to be in favor of a reinterpretation rather than of a compensation.

Certain observations made in the course of the experiments give an interesting insight into the relation between the disparity factors and the unocular factors in the act of vision. It has, of course, long been known that the unocular factors and the memory values of past experience mold to a large extent the interpretation given to the clues arising from the stimulation of disparate retinal elements.¹³ But the developments in the research on aniseikonia and especially the construction of the size lenses which produce a magnification without causing a refractive change provide means by which this interrelation can be far better investigated than was heretofore possible.

The experiments with artificially introduced meridional size differences confirm the well known fact that the disparity factors are the more fundamental ones. Yet

13 "Any one who knows how pliable our spatial visual perceptions are under the influence of various conditions of observation and under the influence of past experience, taken into account consciously or unconsciously, should not be surprised at the multiplicity of results of observations on different objects and with different observers" (Erggellet *Brillenlehre*, in Schieck, F., and Bruckner, A. *Kurzes Handbuch der Ophthalmologie*, Berlin, Julius Springer, 1932, vol 2, p 805.)

they also show that the disparity factors can be largely disregarded when abundant perspective factors are present in a person's surroundings, but that they become immediately operative when the perspective factors are scanty. Fatigue seems to reduce the faculty to disregard the disparity factors, and sleep apparently wipes out to some extent the recent memory values created by a reinterpretation of the relation of objects in space.

Two further conclusions of broad significance are suggested by the experiments. One is based on the fact that it makes a difference in the decrease in effectiveness of the size lenses whether the image of the right or the left eye is magnified in the horizontal meridian. At first this result is rather startling, one would not expect such a difference, since the effect of aniseikonia on spatial localization depends solely on the ratio of the sizes of the two ocular images. But since such a difference was found to be an experimental fact, it must be assumed that different "weight" is given to the two eyes with respect to the response to disparity and unocular clues. This difference in reaction may have some connection with the ocular dominance.

The second conclusion is closely related to the first and concerns individual differences in the response to disparity and unocular factors. Some persons with normal binocular vision are more apt to let the unocular factors influence the spatial localization derived from disparity clues than others, in whom the disparity clues dominate. The latter persons seem to be the ones whose ocular condition shows the least deviation from the normal. It may be possible to establish a typology of visual characters on the basis of the response to the unocular and binocular factors.

The results of the experiments also have some bearing on the explanation of the metamorphopsias and their gradual disappearance. Wilhelm Wundt¹⁴ discussed his own case of disseminated choroiditis of the right eye, which affected the region of the posterior pole of the eye but spared the fovea itself. At first he noticed a pronounced metamorphopsia, which disappeared gradually, leaving only minor irregular distortions at the edge of the diseased area near the macula. Wundt also mentioned the metamorphopsia introduced by prisms and quoted O. Schwarz, who stated:

In a case in which prismatic glasses base out were given for so-called dynamic convergence, an interesting fact was noted. After the glasses were worn for a while, the distortions, noticed at first, disappeared. Yet as the glasses were removed, they reappeared, but in a direction opposite to the one experienced previously, these distortions also disappeared after a while.¹⁵

Wundt considered the disappearance of the metamorphopsias to be a proof of the empiristic theory of spatial localization. He argued that the retinal elements dislodged by the disease of his right eye could not have returned to their exact original position after the disease had healed and scars had formed. Only an acquired change in the relative visual directions could, in his opinion, explain the disappearance of the metamorphopsia. Similar deductions would apply to the distortions produced by prisms, especially in view of the fact, justly emphasized by Wundt, that distortions opposite in direction to the original ones occur when the prisms are removed.

But one does not have to resort to such a sweeping conclusion as a change in the innate relative visual directions of the retinal elements to explain the

¹⁴ Wundt, W. *Zur Theorie der räumlichen Gesichtswahrnehmungen*, Philosophische Studien, Leipzig, W. Engelmann, 1898, vol. 14, p. 1.

¹⁵ James J. Gibson (Gibson, J. J. *Adaptation, After-Effect and Contrast in the Perception of Curved Lines*, *J. Exper. Psychol.* 16:1 [Feb.] 1933) reports experiments along the same lines.

phenomena. The experiments in which a meridional size lens was worn which at first produced distortions analogous to the ones described by Wundt clearly indicate that no change in the relative visual directions of the retinal elements takes place, since the distortions can be shown to be always present in appropriate surroundings, although they disappear completely under ordinary circumstances. The complete disappearance of the metamorphopsias, like the disappearance of the distortions introduced by meridional size lenses, can be fully explained on the basis of a reinterpretation of the relation of objects in space under the influence of unocular factors. This is a process of learning but a very different one from that which Wundt had in mind. In fact, the results reported in this paper not only demonstrate the relative importance of and the part played by the disparity factors and the unocular factors in spatial orientation but open up a possibility for a direct experimental check on the validity of the nativistic theory of space perception.

It may now be attempted to answer the questions raised with regard to spontaneous aniseikonia in the introductory chapter of this paper. Why is it that complaints about disturbances of spatial localization on the part of patients with aniseikonia are extremely rare, in spite of the fact that aniseikonia always entails a disturbance of space perception? How, then, does aniseikonia affect a person's functioning within space?

From the experiments reported in this paper it may be inferred that patients with aniseikonia handle the distortions which necessarily arise from their condition in the same way in which the observers handled the artificially introduced meridional size difference. They disregard largely the disparity factors and rely on the perspective clues. But they have not actually compensated for their aniseikonia, or at least have compensated for only a fraction of it. Nor have the relative visual directions of the retinal elements undergone any change. Because as soon as the patients are placed in artificial or in natural surroundings in which there is a minimum of unocular factors the distortion of the relation of objects in space characteristic of the type of aniseikonia which the patients have becomes at once apparent.⁷ Aniseikonia is in this respect, as in many others, comparable to the heterophorias in that its spatial effects remain latent in ordinary surroundings but become manifest under appropriate conditions, just as the heterophorias become manifest only after fusion is suspended. A person with aniseikonia will have no trouble in ordinary surroundings, but under certain special conditions, and especially when tired, he may experience considerable disturbance in proper functioning in space.

Similar considerations apply to the remark which is sometimes heard that it is superfluous to correct aniseikonic defects, since most people can get accustomed to even larger differences in the size of the ocular images than are currently corrected by iseikonic lenses.

It is, indeed, well known that all spectacles, while achieving the main purpose of providing optimum vision for distance, introduce at the same time a number of radical changes in the visual act of the wearer. Not only is the size of the retinal images changed, as compared with that of the emmetropic eye or with the (sharp or blurred) image the wearer had previous to the correction of his refractive error. The directions in which object points appear in indirect vision are also changed, and with them the field of vision and perspective, so that the size of the objects as well as the interpretation of spatial relations must necessarily be different with and without spectacles. The accessory effects of spectacles on spatial orientation are more pronounced when there is even a small difference in the refractive condition of the two eyes, especially a difference in the astigmatic

error¹⁵ The result is an unusual, often distorted, appearance of the environment when new spectacles are first put on, but soon the wearer becomes accustomed to his glasses and the appearance of his environment returns to normal. This process of adaptation, also, is one not of compensation but only of reinterpretation, since it can be shown with instruments such as the space eikonometer that an incorrect spatial localization introduced by the spectacles will persist no matter how long the glasses are worn. The correct spatial orientation achieved with isekonic lenses would in itself justify their use, even if it were not for other indications for their clinical application.

SUMMARY

Experiments are reported in which 3 observers wore a meridional size lens at axis 90 in front of one eye for eight to fourteen days.

While they were wearing the lens definite discomfort (eyestrain, nervous tension, etc.) was experienced by the observers.

At first the size lens caused the typical disturbance in spatial orientation which would be expected from such a lens, but this disturbance gradually diminished until the usual surroundings, abundant in unocular clues, assumed a normal appearance.

However, even after this adaptation had taken place, the disturbance in spatial orientation became immediately manifest when the observer was placed in surroundings lacking in unocular clues, and quantitative determinations with instruments such as the horopter apparatus and the standard and space eikonometers always showed the greater part of the image size difference to be present.

But after the lens was worn for some time there became manifest a decrease in the amount of the measured image size difference ranging from one fifth to two thirds. The amount of the decrease varied with the person and with the eye in front of which the size lens was worn. There also were certain diurnal variations. The sensitivity to additional size lenses at axis 90 was not influenced by the wearing of the lens.

The question as to the nature of the decrease in the measured image size difference is brought up. The experimental evidence in favor of each of the two possible explanations—psychologic adaptation and physiologic compensation—is discussed.

Measurements made with an instrument with a rotating frontal plane showed a marked difference between different observers in the response to size lenses when perspective patterns were used. This difference permits a classification of subjects according to whether they give more weight to unocular or to binocular factors in their field of view. It would appear that the better a subject's binocular cooperation the more he is likely to respond to disparity factors.

The implications of the results obtained are discussed with regard to the theory of space perception and with regard to the metamorphopsias.

The results of the experimental investigation are applied to the question as to how patients with spontaneous, clinically significant aniseikonia deal with spatial orientation. It is pointed out that such patients may more or less completely adapt themselves to the disturbance in spatial orientation in ordinary surroundings abundant in unocular factors. However, they cannot actually compensate for their image size difference, or at least can compensate only for a fraction of it.

Prof. Adelbert Ames Jr. and Prof. Kenneth N. Ogle advised in this work, and Mr. Robert E. Bannon and Mrs. Mary Beebe acted as observers.

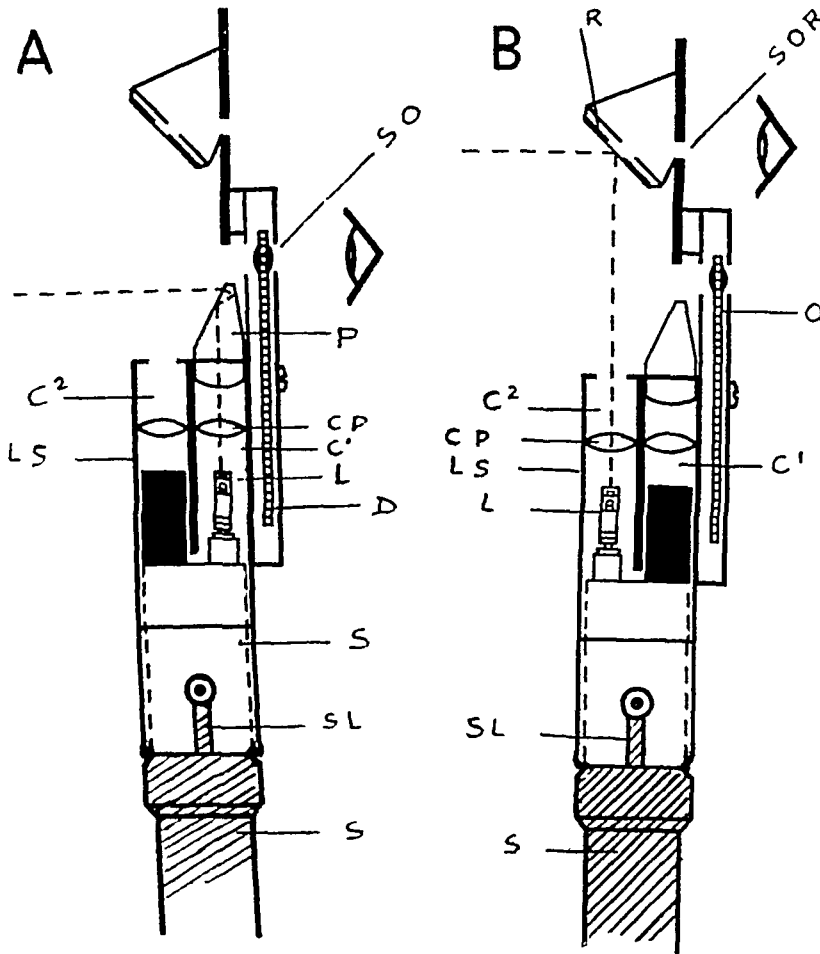
Dartmouth Eye Institute

Clinical Notes

A COMBINED OPHTHALMOSCOPE AND RETINOSCOPE

MAJOR LOUIS K PITMAN, MEDICAL CORPS, ARMY OF THE UNITED STATES

The May electric ophthalmoscope is the instrument most generally used. The light, derived from a lamp with a loop or a curled filament, is fixed on the end of a stem projecting from a battery handle. The tube of the head of the ophthalmoscope, within which this stem is adjustably mounted, holds a condensing lens and a reflecting prism. This lens and prism project the light from the lamp into the



A, ophthalmoscope, and *B*, retinoscope. *L* is the lamp, which is in the posterior chamber, *C*¹, in *A* and in the anterior chamber, *C*², in *B*, *CP*, the condensing lens, *D*, the dial frame holding the lenses, *LS*, the tube, *P*, the reflecting prism, *R*, the reflecting surface, *S*, the stem, *SL*, the slit, *SO*, the sight opening for the ophthalmoscope, and *SOR*, the sight opening for the retinoscope.

eye. Behind the reflecting mechanism is a lens disk provided with a series of lenses, concave and convex, which follow each other in regular order from weaker to stronger. Each lens can be placed in the sight opening, located above the level of the reflector, by manipulating the milled edge of the disk. Opposite each lens is an illuminated number, indicating its strength in diopters.

From the Station Hospital, Eye, Ear, Nose and Throat Service, Basic Training Center no 10, Army Air Force Technical Training Command, Colonel Robert J Platt, Commanding Officer

The electric retinoscope has a lamp mounted on a stem similar to that of the ophthalmoscope. The stem is adjustably mounted within the tube of the retinoscope head. The light rays pass through a condensing lens toward a plane or a concave reflecting surface having a sight opening in the center. The light is thrown into the eye at a distance of 1 meter.

An efficient unit head combining the ophthalmoscope and the retinoscope will eliminate an extra instrument, with saving of material and lowering of the cost of the instrument.

The accompanying schematic drawing shows a cross section of a combined ophthalmoscope and retinoscope head. The tube, *LS*, of the unit head is divided into compartments, *C*¹ and *C*², each holding a condensing lens, *CP*. The stem, *S*, carrying the lamp, is bifurcated at its end. One stem of the bifurcation carries the lamp, *L*, while the other stem is blank (black). There are two opposite slits, *SL*, in the wall of the tube. The stem, *S*, carries a set screw at its side. When the stem, *S*, is mounted within the tube and the set screw is passed through one slit, the lamp will be brought into the posterior chamber, *C*¹ (figure *A*). In order to bring the lamp, *L*, into the anterior chamber, *C*², the stem is drawn out, the set screw being released from the slit, and is then rotated 180 degrees, this permits the screw to be locked into the opposite slit.

The posterior chamber fulfils the function of the ophthalmoscope, for the light passes through the condensing lens and the reflecting prism into the eye (figure *A*). The sight opening *SO* is used.

When the lamp is in the anterior chamber, the retinoscope portion of the instrument comes into use (figure *B*), for the light passes through the condensing lens, *CP*, toward the plane or concave reflecting surface, *R*, and into the eye. The sight opening *SOR* is used.

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Ophthalmologic Reviews

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VISUAL IMPAIRMENT DURING TRYPARSAMIDE THERAPY

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In the second year after the synthesis of tryparsamide had been accomplished, Pearce and Brown¹ noted experimentally that the therapeutic use of the drug was not associated with organic or functional disturbance and, further, that "a definite effect was produced upon the course of the *Treponema* infection due to the peculiar manner in which the drug modified or controlled the infection." In 1924 these investigators² further characterized tryparsamide as having "comparative freedom of untoward effect, moderate treponemacidal action, high tissue penetrability, and the ability to reinforce the powers of natural resistance." Tryparsamide is firmly established as an essential modern agent in the therapy of neurosyphilis, and at least certain of these early noted factors have been substantiated by the clinical experience of the intervening period. With regard to the visual aspects of tryparsamide therapy, however, there has been a persistent lack of accord in opinion. When Lorenz and associates³ introduced tryparsamide into the clinical treatment of neurosyphilis in 1923 admonition was made that damage to the visual system might be associated with its use. Since that time the deleterious effect of tryparsamide on the visual system has been the subject of intensive clinical and experimental observation and controversy, as represented by a voluminous literature comprehending separate phases of the problem. Elucidation of the process, the character and the frequency of untoward visual effects of tryparsamide has remained incomplete, as have satisfactory criteria regarding the ocular contraindications to therapy with the drug in neurosyphilis. The formulation of such criteria, requiring the satisfactory correlation of the factors of altered physiology of vision, pathologic changes in the optic nerve and virulence of the infection, and evaluation of the toxicity of and idiosyncrasy to the drug are complicated by the inadequacy or inaccessibility of much clinical and pathologic material. It is an unfortunate fact that many of the largest statistical collections and clinicoanalytic summaries presenting data derived from the use of tryparsamide refer satisfactorily only to the effect of the drug on neurosyphilis, by even lenient standards, adequate data regarding ocular conditions prior to coincident with and subsequent to this type of therapy are frequently absent, owing certainly, to the unexpectedness of many visual reactions, the occult and delayed character of other types of visual involvement, the similarity of syphilitic and tryparsamide-produced effects and the difficulties inherent in detailed and prolonged routine observation by both the ophthalmologist and the syphilologist. As indication of the diversity of opinion, the reports of

1 Pearce, L, and Brown, W H. Chemotherapy of Trypanosome and Spirochaete Infections. *J Exper Med* **30** 417, 455 and 483, 1919

2 Brown, W H, and Pearce, L. Tryparsamide. Its Actions and Uses, *J A M A* **82** 5 (Jan 5) 1924

3 Lorenz, W F, Loevenhart, A S, Bleckwenn, W J, and Hodges, F J. Therapeutic Use of Tryparsamide in Neurosyphilis, *J A M A* **80** 1497 (May 26) 1923

Tennent⁴ (50 cases), Hyder⁵ (22 cases), Dawson⁶ (20 cases), Lichtenstem⁷ (76 cases), Wolfsohn and Leiva⁸ (37 cases) and Skoog⁹ (50 cases) provide little evidence that use of tryparsamide is a threat to the visual system, while Bleumel and Grieg¹⁰ noted disastrous results in 10 of 50 cases and characterized the drug as "therapeutic dynamite"

Sutherland-Campbell¹¹ has summarized the ocular problem of the use of tryparsamide as follows

This vacillation in the condemnation and advocacy of a drug is to be expected in view of the fact that tryparsamide is generally conceded to be the most efficacious drug used in the therapy of generalized neurosyphilis, while little is known concerning the mechanism of the production of amblyopia as induced either by syphilis or by the pentavalent arsenical

The ocular problems associated with tryparsamide therapy lend themselves to general outline as follows: first, the ocular effects of tryparsamide when pre-existing syphilitic disease of the optic nerve is present, second, the designation of lesions according to whether the damage to the retina or optic nerve is primarily the result of syphilis, of therapy with tryparsamide or of factors introduced by the use of tryparsamide during a period of inactive or active involvement of the optic nerve in a syphilitic process (Jarisch-Herxheimer reaction), third, evaluation of objective and subjective findings with regard to modification of tryparsamide therapy, fourth, evaluation of factors of individual doses, number of injections and subsequent series of injections, fifth, the nature of the reaction to tryparsamide from the visual aspect, and, sixth, the nature of the tryparsamide reaction from the pathologic aspect

THE DRUG

Tryparsamide is the sodium salt of *N*-phenylglycinamide-*p*-arsonic acid. Synthesized in 1917 by Jacobs and Heidelberger,¹² of the Rockefeller Institute, it is a white crystalline powder, 1 Gm of which will dissolve in 1 cc of water to produce an alkaline solution. The arsenic content in the pentavalent form is 25.32 per cent. The drug is of extremely low toxicity when given by intravenous or intramuscular injection, its clinical use is frequently associated with a systemic tonic or mild stimulant effect.

Voegtlin, Smith, Dyer and Thompson¹³ demonstrated experimentally that tryparsamide penetrates into the tissues of the central nervous system. Fordyce and Myers¹⁴ could not demonstrate such unusual penetrative power, examination

4 Tennent, T. Investigations into the Prolonged Treatment of General Paralysis with Tryparsamide, *J Ment Sc* **77** 86, 1931

5 Hyder, H. P. Tryparsamide in Neurosyphilis, *M J & Rec* **121** 475, 1925

6 Dawson, W. S. Treatment of General Paralysis and Tabes by Tryparsamide, *Lancet* **1** 1072, 1925

7 Lichtenstem, J. V. Tryparsamide Therapy, *Arch Dermat & Syph* **24** 182 (Aug) 1931

8 Wolfsohn, J. M., and Leiva, C. Clinical and Serologic Studies of Neurosyphilis with Tryparsamide Therapy, *J A M A* **85** 494 (Aug 15) 1925

9 Skoog, A. L. Tryparsamide Therapy in Neurosyphilis, *J Missouri M A* **22** 387, 1925

10 Bleumel, C. S., and Grieg, W. M. Results Obtained with Tryparsamide in Fifty Cases of Neurosyphilis, *Colorado Med* **22** 16, 1925

11 Sutherland-Campbell, H. Value of Tryparsamide in Treatment of Atrophy of Optic Nerve Due to Syphilis, *Arch Ophth* **24** 670 (Oct) 1940

12 Jacobs, W. A., and Heidelberger, M. Aromatic Arsenic Compounds, *J Am Chem Soc* **41** 1581, 1917

13 Voegtlin, C., Smith, M. I., Dyer, H., and Thompson, J. W. Penetration of Arsenic in Cerebrospinal Fluid, *Pub Health Rep* **38** 1003, 1923

14 Fordyce, J. A., and Myers, C. N. Quantitative Studies in Syphilis from a Clinical and Biological Point of View, *Am J Syph* **9** 490 1925

of the spinal fluid of patients receiving a routine type of tryparsamide therapy showed the complete absence of arsenic in 14 per cent. In other patients the amount of arsenic did not exceed that obtaining in treatment with other arsenical preparations. In order to obtain a level of arsenic in the cerebrospinal fluid comparable to that of silver arsphenamine, it was necessary to introduce seven and one-half times as much tryparsamide. Further, they noted that owing to the rapid excretion of tryparsamide the amount of arsenic available for penetration after the expiration of twenty-four hours was practically negligible. It is their conclusion that therapeutic penetration is hypothetical in that other factors may be involved. Cornwall, Bunker and Myers¹⁵ determined that the maximum amount of arsenic recoverable from the spinal fluid after therapeutic administration of tryparsamide was 7.8 mg per hundred grams. This amount was comparable to that noted for arsphenamine and for neoarsphenamine but was considerably less than that obtained in silver arsphenamine therapy. It was suggested that the favorable clinical results that have been reported in neurosyphilis as a result of treatment with tryparsamide must be ascribed to factors other than the actual quantity of arsenic that enters the spinal fluid.

Basing their conclusion on their clinical experience with tryparsamide, and recognizing the low treponemacidal action of tryparsamide as compared with the arsphenamines, Moore, Robinson and Lyman¹⁶ stated in 1924 that the use of tryparsamide in the treatment of syphilitic states other than neurosyphilis was precluded, a view more recently substantiated and applied to the clinical use of the drug.¹⁷

Moore^{17a} outlined the clinical use of tryparsamide in neurosyphilis as follows. The drug is contraindicated except in the treatment of neurosyphilis, for which it is usually used after six months of preliminary treatment with arsphenamine. The average, and the maximum, dose is 3 Gm given intravenously, although there may be some advantage in the use of an initial dose of 1 Gm the first week, 2 Gm the second week and 3 Gm each succeeding week. A minimum course consists of twelve weekly injections, although the course may be prolonged indefinitely. Prolonged use of the drug is usually productive of better results.

PRIMARY SYPHILITIC ATROPHY OF THE OPTIC NERVE

According to the statistical studies of Woods and Dunn¹⁸ and Woods and Rowland,¹⁹ primary atrophy of the optic nerve may be recognized not only as the most frequent neuropathy (71 per cent), but as most frequently due to syphilis (41 per cent). Igersheimer²⁰ has noted that 10 to 15 per cent of all patients with tabes dorsalis ultimately have atrophy of the optic nerve, which has been described²¹ as "probably the most resistant feature of the most resistant form of neurosyphilis, i. e., tabes dorsalis." Usually unaccompanied by other syphilitic

15 Cornwall, L. H., Bunker, H. A., and Myers, C. N. Arsenic in the Spinal Fluid, *Arch Neurol & Psychiat* **25** 137 (Jan) 1931.

16 Moore, J. E., Robinson, H. M., and Lyman, R. S. Results of Tryparsamide Therapy in Syphilis, *J A M A* **83** 888 (Sept 20) 1924.

17 (a) Moore, J. E. *The Modern Treatment of Syphilis*, Springfield, Ill., Charles C. Thomas, Publisher, 1941. (b) Stokes, J. H. *Modern Clinical Syphilology*, Philadelphia, W. B. Saunders Company, 1934.

18 Dunn, J. R., and Woods, A. C. Etiology Study of a Series of Optic Neuropathies, *J A M A* **80** 1113 (April 21) 1923.

19 Woods, A. C., and Rowland, W. M. Etiologic Study of a Series of Optic Neuropathies, *J A M A* **97** 375 (Aug 8) 1931.

20 Igersheimer, J. *Syphilis und Auge*, Berlin, Julius Springer, 1918, Ueber der Opticusprozess bei Tabes und Paralyse, *Deutsche med Wchnschr* **52** 943, 1926.

disease of the eye, the process may be completed in several months or delayed by remissions over a period of several years. Optic nerve atrophy usually develops during the preataxic state, together with pupillary changes, the pallor of the disk appears first in the temporal portion but may quickly involve the entire nerve head. An extremely important observation with direct application to the problem of trypanamide therapy was contributed by Traquair,²¹ Dworjetz,²² Somberg²³ and others, who noted that there is no relationship of either qualitative or quantitative character between the appearance of the nerve head and the functional capacity of the optic nerve. An appearance of atrophy may be associated with normal visual function, or, conversely, in developing atrophy, vision may be largely destroyed prior to ophthalmoscopic changes in the nerve head.

Stargardt²⁴ described the histopathologic changes of primary syphilitic optic nerve atrophy as glial proliferation in the nerve and the appearance of plasma cells in the contiguous pia, earliest involvement was noted in the chiasmatic region, and a similar process later appeared in the intracranial portion of the nerve, single or multiple areas being involved with dissimilar rates of progression. Once initiated the process consisted of progressive pial infiltration and glial proliferation, beneath infiltrated pial areas medullary sheaths showed marginal degenerative changes, which soon involved axis-cylinders, these being ultimately replaced by glial cells filled with amyloid. Intraneural connective tissue and blood vessels were not involved in the process even though far advanced atrophy was present. The relationship of the processes of inflammation and degeneration has remained obscure, apparently as summarized by Moore,²⁵ the pathologic changes of primary atrophy are at first inflammatory and ultimately degenerative, the degenerative apparently being due to factors such as nutrition. Hauptmann²⁶ presented the assumption of a toxin mechanism of extracranial origin which produced degenerative changes through a selective action on the optic nerve, Wilbrand and Saenger²⁷ classified syphilitic involvement of the optic nerve as a simple perineuritis of the orbital and periorbital nerve. Neither of these explanations of the process is wholly tenable in view of the present understanding of the syphilitic process.

In the pia and arachnoid of the intracranial portion of the nerve, Igersheimer²⁰ has observed the presence of *Spirochaeta pallida* in equal numbers of cases of inflammatory changes of the nerve without degeneration and of optic nerve atrophy. On the other hand, production of optic nerve lesions by forms of *S. pallida* not yet microscopically identified (Saleeby and Greenbaum²⁸) is worthy of deliberation.

That all atrophy of the optic nerve occurring when the serologic reactions are positive is not of the primary type was indicated by Igersheimer,²⁰ who enumerated additional ways in which atrophy may be produced by syphilis in association with severe chorioretinitis of congenital syphilis, following the severe inflammatory reaction of acquired syphilis (in this instance the atrophy may be secondary),

21 Traquair, H. M. Clinical Differentiation of Various Forms of Optic Atrophy, *Brit M J* **2** 1157, 1922.

22 Dworjetz, M. Atrophie Nervi Optici, *Klin Monatsbl f Augenh* **80** 30, 1928.

23 Somberg, J. S. Optic Nerve Pallor Without Functional Defects in Luetics, *Am J Ophth* **10** 837, 1927.

24 Stargardt, K. Ursachen des Sehnervenschwundes, *Arch f Psychiat* **51** 711, 1913.

25 Moore, J. E. Syphilitic Optic Atrophies. *Medicine* **11** 263, 1932.

26 Hauptmann, T. Theorie auf Grund neuerer Forschungsergebnisse, *Ztschr f d ges Neurol u Psychiat* **128** 107, 1930.

27 Wilbrand, H., and Saenger, A. Die Neurologie des Auges, Wiesbaden, J. F. Bergmann, 1913.

28 Saleeby, E., and Greenbaum, S. Comparative Biologic and Histologic Study of Lymph Glands from Syphilis Patients, *J A M A* **96** 98 (Jan 10) 1931.

accompanying gumma or periostitis of the orbit with pressure on the nerve, resulting from papillitis in basilar syphilitic meningitis, and following the pressure of syphilitic inflammatory products on the pathway from the orbit to the external geniculate bodies. By implication, then, atrophy of the optic nerve cannot always be designated as primary or secondary on the basis of ophthalmoscopic examination alone.

THE VISUAL FIELDS IN ATROPHY OF THE OPTIC NERVE

Moore²⁵ has suggested that field changes occur very likely as the initial clinical evidence of optic nerve atrophy and certainly before pallor of the optic disk is noted, such a suggestion, he pointed out, is a conjecture substantiated by frequent observation and by the comments of Igersheimer²⁰ who designated the first alteration of vision associated with syphilitic primary atrophy of the optic nerve as constriction of the visual fields for white and color, occurring prior to involvement of central vision. Either concentric (regular or irregular) contraction or sector-shaped defects were encountered, with the fields for color showing a type of defect similar to that of the field for form. Constriction of the fields for color occasionally preceded alteration of the field for form, with progressive loss first of green, then of red and finally of blue. Depression of green perception was held to imply involvement of the whole cross section of the nerve. Enlargement of the blindspot was described as an additional early symptom.

That there actually is a type of visual field characteristic of atrophy of the optic nerve was questioned by Uthoff,²⁹ who designated two general types. In the first, perimetric reduction of the fields for form and color was associated with loss of both central and peripheral acuity, red-green perception was early involved, in contrast to blue-yellow perception, which was somewhat longer preserved. Such findings were presumed to be indicative of involvement of the entire cross section of the nerve. In the second type, abnormal portions of the visual field were sharply delimited from areas of normal function, sector defects and marked contractions of the field occurred. However, visual acuity and color sense were not implicated in the process, apparently because of a relative sparing of fibers serving the central portion of the retina. Circumferential syphilitic involvement of the optic nerve proper was assumed in the latter type of visual field. The possibility that sparing of the central portion of the retina was explained by the greater relative number of fibers supplying this region was suggested by Ronne,³⁰ who indicated that disproportionate loss of central and color vision might be best explained as loss of function of fibers subserving but a single function. Such disproportionate involvement, when occurring, was considered as an especially unfavorable indication of progression.

Uthoff, quoted by Wilbrand and Saenger,²⁷ noted homonymous hemianopsia in 11 of 100 cases. This type of field is ascribed to syphilitic degeneration of vessels with secondary cerebral involvement, gummatous meningitis or syphilitic tumor of the optic tracts, Lissauer³¹ and Marie³² have noted it in dementia paralytica. Lillie³³ suggested that the appearance of homonymous hemianopsia in

29 Uthoff, W. Die Augenveränderungen bei den Erkrankungen des Nervensystems, in Graefe, A., and Saemisch, E. T. Handbuch der gesamten Augenheilkunde, ed 2, Leipzig, Wilhelm Engelmann, 1909.

30 Ronne, H. Die Prognose der Sehnervenatrophie, Klin Monatsbl f Augenh 49 154, 1911.

31 Lissauer, cited by Wilbrand and Saenger,²⁷ 1917, vol 7.

32 Marie, cited by Wilbrand and Saenger,²⁷ 1917, vol 7.

33 Lillie, W. I. Tryparsamide Treatment of Syphilis of the Nervous System, J A M A 83 809 (Sept 13) 1924.

tabes dorsalis be regarded as due to "concurrent florid syphilis or to arteriosclerosis", another type of defect, described by Lillie³⁴ as a "palpebral slitlike contraction," was described as being associated with syphilitic perineuritis of the optic nerve

Arlt³⁵ classified the field defects of syphilitic patients as contraction for form and color, with reduction of central visual acuity, 85 per cent, sector-shaped defects, 9 per cent, and central scotoma, 6 per cent. With regard to central scotomas in syphilitic patients, von Hippel²⁷ has pointed out that they may frequently be more accurately ascribed to the amblyopia of alcohol, tobacco, sinus disease or diabetes than to tabes

In classifying the field defects of 56 patients with a clinical diagnosis of primary syphilitic atrophy of the optic nerve, Sloan and Woods³⁶ designated concentric peripheral contraction in 7, a localized defect of the peripheral field in 19, central or cecocentral scotoma with normal peripheral fields in 8 and central or cecocentral scotoma with contracted fields in 22. In this series, central or cecocentral scotoma was present in over 50 per cent. Homonymous hemianopsia, previously referred to, was not noted as a visual field change associated with optic nerve atrophy and tabes dorsalis. This clinical study of 56 selected patients is the most complete investigation of its nature available in the literature, summarizing their material, Sloan and Woods³⁶ have been able to draw a remarkably close parallel between their clinical findings and the available pathologic data, already considered. It was noted that the primary lesion was certainly not behind the chiasm, further, bilateral symmetry of field defects was ascribed to multiple lesions of the optic nerve. They noted that if fibers supplying the peripheral portion of the retina have a peripheral location in the nerve, then various forms of field defects may be explained on the basis of a lesion starting in the periphery of the optic nerve. A diffuse lesion affecting the entire periphery of the nerve would produce concentric contraction of the field. Lesions of the foramen or of the intracranial portion of the nerve would be accompanied with late involvement of the cecocentral area of the field owing to the axial (central) location of the papillomacular bundle. If, however, a diffuse perineural lesion was located near the papilla, where this bundle is peripheral, it would produce a cecocentral scotoma in addition to peripheral contraction. Thus, isolated cecocentral scotomas, nasal steps and combinations of the two defects would result from a lesion in the anterior portion of the nerve which involved the papillomacular bundle, the fibers contiguous to it or both.

Their investigation further indicated that field defects for colored and for small white objects may either regress or completely disappear, a finding considered to be in accord with the conclusion of Stardzajt²⁴ that the primary lesion in syphilitic atrophy of the optic nerve is a peripheral and interstitial neuritis and that actual degeneration of the nerve fibers is secondary to this inflammatory change.

TRYPARSAMIDE THERAPY WHEN PRIMARY SYPHILITIC ATROPHY OF THE OPTIC NERVE EXISTS

If adequate therapy can be attained prior to the complete destruction of the nerve fibers, there is the possibility that the neuritic process may be controlled

34 Lillie, W. I. Peculiar Contraction of Normal Visual Fields Associated with Syphilis of the Central Nervous System, *Tr Am Ophth Soc* 32:153, 1934.

35 Arlt, E. Behandelte und unbehandelte Fälle von tabischen Sehnerven Atrophie, *Ztschr f arztl Fortbild* 19:367, 1922.

36 Sloan, L. L., and Woods, A. C. Perimetric Studies in Syphilitic Optic Neuropathies, *Arch Ophth* 20:201 (Aug) 1938.

or prevented, according to Moore,²⁵ who has contended that antisyphilitic therapy in cases of primary syphilitic atrophy of the optic nerve offers hope only when instituted before visual loss has occurred. Such a comment lends emphasis to the necessity of early and accurate diagnosis of atrophy of the optic nerve. Disregarding the variable factors of remission and course, Moore has noted that not only has arsphenamine proved to be of little value in the treatment of optic nerve atrophy, but there is some indication that the course of degeneration may actually be accelerated, this comment is somewhat modified by the statement of Lillie,³³ who has ascribed renewed involvement of the optic nerve after the use of arsphenamine to a provocative reaction due possibly to inadequate doses of the drug. Lillie has recognized that damage to the optic nerve ascribed to tryparsamide may in many instances be a continuous degenerative syphilitic process. This view is based on the observation of 13 patients with visual disturbance (in 4 of these the disturbance was severe) among 114 patients receiving tryparsamide therapy. Examination of the visual fields of both tryparsamide-treated and untreated patients with optic nerve atrophy showed a similarity so marked that Lillie was able to conclude that visual damage was actually greater in the untreated patients than in the patients treated with tryparsamide and, further, that tryparsamide is no more harmful to the visual apparatus than either arsphenamine or sulfarsphenamine (Parsons' ³⁷ experience with sulfarsphenamine does not incline him to this view). Neff ³⁸ has summarized the results of treatment of 15 patients who had definite syphilitic ocular lesions prior to the use of tryparsamide, it is his conclusion that preexisting disease of this character does not adequately establish a contraindication to the use of tryparsamide.

In a study of 27 patients with all types of syphilitic ocular lesions prior to the use of tryparsamide, Cady and Alvis ³⁹ noted the following results: 37 per cent became worse, 14.8 per cent improved and the lesions of 48.2 per cent did not change. Of the patients with optic nerve atrophy, treated with tryparsamide, as many progressed toward blindness as were not affected. The conclusions of these authors indicate that tryparsamide may be used with close observation if syphilitic disease of the optic nerve or syphilitic ocular disease is present. When mild deleterious effects from tryparsamide occur, discontinuance of treatment for one month was recommended, with resumption of treatment after the expiration of that interval.

A contrary view is presented by O'Leary ⁴⁰ and by Moore, Robinson and Keidel,⁴¹ who have concluded that syphilitic disease of the optic nerve does establish a contraindication to therapy with tryparsamide, a view apparently shared by Lorenz and associates ⁴³. Lees ⁴⁴ treated 21 patients with established optic nerve

37 Parsons, R. P. Tryparsamide and Sulpharsphenamine in Treatment of Neurosyphilis, U. S. Nav. M. Bull. **22** 526 (May) 1925.

38 Neff, E. E. Effect of Tryparsamide on Optic Tract, Wisconsin M. J. **24** 120, 1925.

39 Cady, L. D., and Alvis, B. Y. Use of Tryparsamide in Patients With and Without Ocular Lesions, J. A. M. A. **86** 184 (Jan. 16) 1926.

40 O'Leary, P. A. Present-Day Status of Treatment of Neurosyphilis, J. A. M. A. **109** 1163 (Oct. 9) 1937.

41 Moore, J. E., Robinson, H. M., and Keidel, A. Tryparsamide in Treatment of Syphilis, J. A. M. A. **82** 528 (Feb. 16) 1924.

42 Footnote deleted.

43 Lorenz, W. F. The Treatment of Central Nervous System Syphilis with a New Arsenical, Wisconsin M. J. **20** 336, 1922. Lorenz, W. F., Loevenhart, A. S., Reitz, T. F., and Eck, C. P. Use of Tryparsamide in Neurosyphilis, Am. J. M. Sc. **168** 157, 1924.

44 Lees, D. Use of Tryparsamide in the Treatment of Syphilitic Optic Atrophy, Tr. Ophth. Soc. U. Kingdom **52** 203, 1932.

atrophy with tryparsamide and ascribed further deterioration of vision in 5 (severe and rapid in 2) to the direct action of the drug. Perhaps the most closely controlled series from the ophthalmologic standpoint was presented by Mayer and Smith,⁴⁵ who observed deleterious results in 3 of 14 patients with primary syphilitic atrophy of the optic nerve treated with tryparsamide, 2 of these patients recovered satisfactorily, but 1 case showed permanent contraction of the visual fields without impairment of central vision or alteration of the color of the nerve head. This series comprised 87 patients, and the authors concluded that "tryparsamide, intelligently administered, causes no increase in the atrophy of the optic discs, where syphilis has previously caused changes" and "causes no optic atrophy where the action of syphilis has not affected the discs."

The stringent ocular contraindications to the treatment of syphilis elaborated by Behr (quoted by von Hippel⁴⁶) are, first, diminished central vision or loss of color vision with normal or near normal fields, second, concentric contraction of the fields both for form and for color with central vision normal, third, transitory visual field disturbance, especially in form, with normal central vision and optic nerve atrophy, and, fourth, subjective visual complaints. Von Hippel has commented that these restrictions exclude most patients with syphilis from therapy.

Woods and Moore⁴⁷ have indicated that preexisting syphilitic disease of the optic nerve or retina is not necessarily a contraindication to therapy with tryparsamide, this view is, however, modified by the comment that once evidence attributable to tryparsamide is present use of the drug should be discontinued. They have shown, also, that deleterious effects may be encountered in the use of tryparsamide in other diseases besides syphilis, namely, postencephalitic Parkinson syndrome, lymphosarcoma and trypanosomiasis.

In an extensive summary of the problem, Sutherland-Campbell⁴⁸ has indicated that there is basis for the view that both the syphilitic virus and tryparsamide have an affinity for the optic tract in certain cases, he stated the belief that the consensus indicates that toxic reactions to tryparsamide therapy occur rarely if the disks and fields are unaffected (by syphilitic disease) and, further, that an abnormality of either the fundi or the visual fields should preclude the use of tryparsamide. He recognized that many ophthalmologists contend that tryparsamide therapy should be employed in spite of changes in the eyegrounds or constriction of the fields. Mayer,⁴⁸ and Cordes in a discussion of Mayer's paper, supported this view. Sutherland-Campbell suggested that the finding of involvement of the optic nerve should contraindicate the use of tryparsamide therapy in general practice until more exact contraindications are available. Whatever measures are eventually adopted in the treatment of primary atrophy of the optic nerve, according to Sutherland-Campbell tryparsamide "stands condemned" of dangerous potentialities in those cases of tabes dorsalis or dementia paralytica in which optic nerve atrophy is present.

45 Mayer, L. L., and Smith, R. D. Ocular Manifestations in Tryparsamide Treatment of Syphilis, *Illinois M. J.* 65:258, 1934.

46 von Hippel, E., in Graefe, A., and Saemisch, E. T. *Handbuch der gesamten Augenheilkunde*, Berlin, Julius Springer, 1923.

47 Woods, A. C., and Moore, J. E. Visual Disturbances Produced by Tryparsamide, *J. A. M. A.* 82:2105 (June 28) 1924.

48 Mayer, L. L. Tryparsamide Therapy of Neurosyphilis and Atrophy of Optic Nerve, *J. A. M. A.* 109:1793 (Nov. 27) 1937.

SUBJECTIVE OCULAR SYMPTOMS DURING TRYPARSAMIDE THERAPY

At the time that tryparsamide was introduced clinically, Loienz and co-workers³ stated that single doses as large as 5 Gm were well tolerated except that transient amblyopia was occasionally produced. Their experimental work had indicated that the drug had an affinity for tissue of the nervous system, apparently for this reason these authors emphasized the fact that tryparsamide possesses the potentiality of injury to the optic tract and advised against administering it to patients showing degenerative changes of the optic nerve. Their later experience⁴³ with a 5 Gm dose of tryparsamide weekly produced transient visual complaints in 40 per cent of their patients, on reduction of the dose to 3 Gm the incidence of an unspecified type of visual disturbance was correspondingly reduced to 7 per cent. Brown and Pearce² noted occasional subjective complaints of dim vision twenty-four to seventy-two hours after the injection of tryparsamide, such symptoms were invariably temporary. Crawford⁴⁹ noted no complaints associated with the administration of the drug when small doses were given and was never obligated to discontinue administration for this reason. Downs and associates⁵⁰ in a closely observed (ophthalmologically) series of 223 patients who received 5,353 injections of 1 to 3 Gm of tryparsamide noted reactions in 93, those in 44 per cent being subjective. Among the patients with subjective symptoms, objective ocular findings were absent. In this series, 78 per cent of the patients noted the subjective effects (dim vision, sparks, distortion, flashes) prior to the tenth injection and 22 per cent after the tenth injection. In all but 1 of the latter group, comprising 9 patients, recurrence of subjective symptoms was noted during subsequent series of injections.

Woods and Moore⁴⁷ noted that 101 per cent of their patients receiving tryparsamide therapy made complaints of visual disturbance, in them, also, objective findings were absent. It was their observation that after subjective symptoms had disappeared even more intensive tryparsamide therapy could be administered without recurrence of a similar type of complaints and, further, the size of the dose apparently had relatively little to do with the production of this type of complaint, in fact, small doses were thought to produce more undesirable visual effects than did the larger doses. They recognized that patients with dementia paralytica or tabes dorsalis noted subjective disturbances more frequently than did patients with other types of neurosyphilis.

Moore and Sutton⁵¹ have emphasized the importance of subjective symptoms in view of the fact that fundus changes and other objective findings are absent at the time subjective complaints are noted.

The administration of tryparsamide to patients who were not ophthalmologically retested despite the appearance of subjective complaints was described by Sloan and Woods⁵². One patient noted a subjective type of reaction after both the third and the eighteenth dose but retained normal vision although there was moderate contraction of the fields. The other patient noted subjective disturbance of vision after the third injection and progressed to blindness on the persistence of treatment. Both ultimately showed optic nerve atrophy, the former slight and the latter marked.

⁴⁹ Crawford, E. M. Tryparsamide Therapy in Neurosyphilis, *Canad. M. A. J.* **15** 46, 1925.

⁵⁰ Downs, W. G., McDermott, W., and Webster, B. Reactions to Tryparsamide Therapy, *Am. J. Syph., Gonorr. & Ven. Dis.* **25** 16, 1941.

⁵¹ Moore, J. R., and Sutton, I. C. Tryparsamide in Treatment of Late Neurosyphilis, *J. Nerv. & Ment. Dis.* **63** 569, 1926.

⁵² Sloan, L. L., and Woods, A. C. The Effect of Tryparsamide on the Eye, *Am. J. Syph., Gonorr. & Ven. Dis.* **20** 583, 1936.

Among 52 patients (Ebaugh and Dickson⁵³) and 100 patients (Solomon and Viets⁵⁴) transient symptoms of unspecified character were noted, in both series, persistence of unfavorable effects was noted in a small percentage of patients treated

In a review of the literature describing the treatment with tryparsamide of 2,087 patients without preexisting syphilitic lesions of the optic nerve, Sloan and Woods⁵² noted an aggregate of 5.33 per cent of subjective reactions. These complaints consisted of dazzling, shimmering or tremor of vision, occurring transiently six to twenty-four hours after the injection, objective findings were absent

Characteristic of the subjective reaction to tryparsamide therapy is the apparent intensification of the visual disturbance in positive illumination with diminution of symptoms in subdued illumination¹⁷

OBJECTIVE IMPAIRMENT OF VISION DURING TRYPARSAMIDE THERAPY

Woods and Moore⁴⁷ observed that 5.5 per cent of their patients showed objective signs of visual damage during therapy with tryparsamide, final studies of this series after use of the drug was discontinued indicated that either complete recovery or severe permanent visual deterioration might result, avoidance of the latter permanent and severe sequela was accomplished by the withdrawal of the drug immediately on the appearance of symptoms. In this particular series of patients 94 per cent of the reactions appeared prior to the tenth injection of the drug and were considered by the investigators to be due to a direct toxic effect of the drug on the nerve or retina. The change in the visual field was described as contraction, involving especially the upper and lower nasal areas, with involvement of the temporal portion occurring infrequently. Among their patients showing unfavorable visual tolerance to the drug, 3 patients attained full recovery, 3 patients had a residuum of slight contraction of the fields (with normal vision), 5 patients had reduced central vision and 2 patients suffered severe permanent damage

Downs and associates,⁵⁰ previously referred to, noted that 52 patients among 223 receiving tryparsamide had objective reactions, of these, 20 patients had reactions described as mild, consisting of moderate contraction of the fields, especially in the nasal portion, together with depression of the visual acuity. The changes disappeared when use of the drug was discontinued. The reactions in 11 patients appeared prior to the tenth injection and those in 9 after the tenth injection. An additional 27 patients had reactions designated as moderately severe, characterized by contraction of the fields and depression of central vision, neither of which type of change was permanent. In this group, the reactions in 17 patients occurred prior to the tenth injection and those in 10 occurred later

Pearce⁵⁵ discussed the use of tryparsamide in 77 patients with trypanosomiasis; objective reactions occurred in 9 but permanent damage was detected in only 3 of these patients. Powell and Smith⁵⁶ described constriction of the fields in 11 of 16 patients during routine administration of tryparsamide. Three patients showed no change, and 5 showed an initial expansion followed by subsequent contraction. Moderate contraction following an initial expansion possibly due to the tonic

53 Ebaugh, F. G., and Dickson, R. W. Tryparsamide in the Treatment of General Paralysis, *J. A. M. A.* **83** 803 (Sept. 13) 1924

54 Solomon, H. C., and Viets, H. R. A Comparison of Tryparsamide and Other Drugs in Treatment of Neurosyphilis, *J. A. M. A.* **83** 891 (Sept. 20) 1924

55 Pearce, L. Studies on Treatment of Human Trypanosomiasis with Tryparsamide, *J. Exper. Med.* **34** 1, 1921

56 Powell, L. S., and Smith, H. S. Studies of Visual Fields in Connection with Tryparsamide Therapy, *Arch. Ophth.* **24** 276 (Aug.) 1940

effect of the drug was considered as a usual occurrence rather than as a reaction to the drug, which did not occur in this series. Among 4 patients with objective reactions among 85 syphilitic patients receiving tryparsamide, Wile and Wieder⁵⁷ noted that in 1, in addition to blurring of the vision, a neuroretinitis with contraction of the fields for form and color developed.

Cady and Alvis³⁹ have noted that statistical studies of poor results are frequently associated with limited numbers of patients, and they have attributed unfavorable visual effects to inadequate experience with the drug. In their closely studied (ophthalmologically) series of patients free of detectable syphilis-produced ocular lesions, only 5.2 per cent manifested involvement due to tryparsamide. Permanent change, however, occurred in only 1.3 per cent of persons who prior to use of tryparsamide were free of optic neuritis, optic nerve atrophy or syphilis-produced change in vision, fundi or visual fields.

Sloan and Woods⁵² noted in their summary (previously referred to) of 2,087 reports in the literature on patients in whom prior syphilitic involvement of the optic nerve was not apparent that 3.53 per cent of the patients presented objective evidence of damage due to tryparsamide. In the reaction which they classified as "chronic," changes are noted primarily in the visual fields, with central vision relatively undisturbed. The upper and lower portions of the fields nasally were involved. Scotomas were not present, nor was either the blindspot or the color vision altered. Constriction of the fields, once developed, tended to be permanent, visual loss usually stopped short of blindness if use of the drug was discontinued.

Sloan and Woods⁵² indicated that the peripheral field defects of tryparsamide therapy and of syphilitic atrophy of the optic nerve are similar in that there is greater contraction proportionally for white than for blue or red and a greater defect for red than for blue, the latter finding being common to all early lesions of the conduction path. Field defects of syphilitic atrophy of the optic nerve do not show relative sparing of the temporal field and contraction of the upper and lower nasal fields, as is consistently the case with tryparsamide. In damage due to tryparsamide the far periphery of the field is affected most severely, the midperiphery only slightly and the central field not at all, except in very severe reactions, this fact indicating a lesion which does not affect the entire cross section of the nerve at the same time. They did not agree with Lillie in his view that the visual field defects accompanying tryparsamide therapy are due to reactivation of a latent syphilitic optic nerve atrophy and suggested that if a direct neuritic involvement of the peripheral nerve occurs the lesion cannot be near the bulb, where the papillo-macular bundle, not usually involved, is located. Infrequency of pallor of the disk supports such a view. Further, if reactivation of the syphilitic process were the explanation of visual involvement, then sparing of the temporal field would not be possible.

Lillie³³ has indicated that the impression of a direct toxic effect due to tryparsamide may be questioned, as such an occurrence should produce loss of central vision due to central scotomas. His understanding of this relationship of tryparsamide to syphilitic disease of the eye has been considered.

Stokes and Wilhelm⁵⁸ noted 8 patients with objective visual reactions among 152 patients and emphasized that normal vision and fundi are compatible with marked constriction of the visual fields. These patients, together with others on

⁵⁷ Wile, U. J., and Wieder, L. M. Tryparsamide in the Treatment of Neurosyphilis, *J. A. M. A.* **84** 1710 (June 6) 1925.

⁵⁸ Stokes, J. H., and Wilhelm, L. F. X. Tryparsamide in the Treatment of Neurosyphilis, *Arch. Dermat. & Syph.* **11** 579 (May) 1925.

whom detailed ocular studies were made, were the basis of a report by O'Leary and Becker,⁵⁹ in which subjective reactions were noted in 14 patients and objective reactions in 9. Among the latter, 5 patients retained permanent damage, in 3 this was contraction of the fields and in 2 homonymous hemianopsia. The reports of Kirby and Hinsie,⁶⁰ Campbell,⁶¹ Gibbs and Reichenbach,⁶² Berg,⁶³ Neymann and Singleton,⁶⁴ Silverston,⁶⁵ Kibler,⁶⁶ Branche,⁶⁷ Lazar,⁶⁸ and Cormia⁶⁹ may be summarized as follows. 413 cases were presented, with the occurrence of objective reactions in 19. In general, the cases were inadequately studied ophthalmologically for statistical purposes. Subjective complaints were not described by the various authors. It is noted that there was an aggregate of 4.5 per cent of objective reactions.

Mayer and Smith⁴⁵ presented a series of 72 patients in whom no indication of syphilitic involvement of the eye was noted, extremely careful ophthalmologic examinations were made at repeated intervals, which included colorimetric estimation of the disk. They were able to detect objective reactions in 5, none had residual loss of vision on follow-up examination.

ALTERATION OF LIGHT SENSE DURING TRYPARSAMIDE THERAPY

In association with objective ocular changes Sloan and Woods⁷² have described the light sense as altered by tryparsamide therapy. It was their preliminary impression, based on the study of 8 patients who received tryparsamide as compared with 77 patients with syphilis of the central nervous system without ocular involvement who did not receive tryparsamide, that a reduction in sensitivity to light occurred in every patient with contraction of the fields or pallor of the disk which followed the use of tryparsamide, and, further, a quantitative evaluation of the severity of the tryparsamide reaction in a few patients seemed to be possible. However a normal curve for certain patients with marked field contraction following tryparsamide therapy suggested that the test is of less value in detecting objective damage than is perimetry. Peripheral meridional measurements, however, were anticipated to show depression of the light sense at the onset of untoward effects of tryparsamide.

ACUTE VISUAL REACTION TO TRYPARSAMIDE THERAPY

Five patients among 223 treated and reported on by Downs and associates⁷⁰ experienced sudden complete loss of central and peripheral vision. The ultimate

59 O'Leary, P. A., and Becker, S. W. Further Observations on the Treatment of Neurosyphilis with Tryparsamide, *M. J. & Rec.* **123** 305, 1926.

60 Kirby, G. H., and Hinsie, L. E. Tryparsamide Treatment of General Paralysis, *State Hosp. Quart.* **12** 53, 1926.

61 Campbell, G. B. Treatment of General Paralysis by the Use of Tryparsamide, *State Hosp. Quart.* **12** 76, 1926.

62 Gibbs, C. E., and Reichenbach, E. B. Tryparsamide in General Paralysis, *State Hosp. Quart.* **12** 82, 1926.

63 Berg, L. Results with Tryparsamide in the Treatment of Neurosyphilis, *Am. J. Syph.* **10** 261, 1926.

64 Neymann, C. A., and Singleton, D. E. Therapeutic Results with Tryparsamide in the Treatment of Neurosyphilis, *J. Nerv. & Ment. Dis.* **64** 144, 1926.

65 Silverston, J. D. Observations on Tryparsamide Therapy in Neurosyphilis, *Lancet* **2** 693, 1926.

66 Kibler, O. The Value of Intensive Treatment with Tryparsamide and Mercury in General Paralysis, *Illinois M. J.* **59** 117, 1931.

67 Branche, G. C. Tryparsamide Therapy of Neurosyphilis in Negroes, *U. S. Vet. Bur. M. Bull.* **7** 476, 1931.

68 Lazar, N. K. Effect of Tryparsamide on the Eye, *Arch. Ophth.* **11** 240 (Feb.) 1934.

69 Cormia, F. E. Tryparsamide in Treatment of Syphilis of the Nervous System, *Brit. J. Ven. Dis.* **10** 99, 1934.

result was permanent contraction of the field and diminished visual acuity. Four of these severe reactions occurred prior to the tenth injection, one occurred after the tenth injection.

King⁷⁰ reported in detail the course of 1 patient with a severe reaction to tryparsamide. There had been no preliminary ocular examination, reduced vision was noted ten days after the third injection, associated with contraction of the fields for white and color and central scotoma in each eye. There was pallor of the disks. In two weeks the vision improved, with disappearance of the central scotoma, but the visual fields remained contracted. The peripheral fields showed progressive contraction, with complete blindness ensuing five months later. Smith⁷¹ noted 2 patients with acute reactions among 45 patients treated with tryparsamide. One of these showed complete recovery in five weeks, the other (with indications of preceding syphilitic damage) showed approximately 50 per cent recovery.

Casten⁷² has described an acute reaction occurring in normal eyes subsequent to the second injection. With forced drainage of the cerebrospinal fluid as immediate treatment, and repetition of the procedure on four occasions, gradual improvement of vision to 20/15 with an expansion of the fields to near normal was noted in four months. Sloan and Woods³⁶ have reported a similar reaction occurring after the administration of 3 Gm of tryparsamide, treatment with typhoid vaccine, malaria inoculations and forced drainage of the cerebrospinal fluid was accomplished with the return of vision from perception of shadow to 20/20 and only moderate depression of the visual fields seven months after visual impairment occurred.

Fine⁷³, Weeks,⁷⁴ Woods and Moore⁴⁷ and Sharpe⁷⁵ have described briefly and without great detail acute reactions to tryparsamide therapy.

Muncy⁷⁶ has advocated the use of vitamin B concentrate in the treatment of acute reactions to tryparsamide, Leinfelder⁷⁷ has not been able to duplicate the reported satisfactory results of return of visual function.

MECHANISM OF TRYPARSAMIDE DAMAGE TO NERVE AND RETINA

Young and Loevenhart,⁷⁸ in studying the experimental toxicity of various arsenicals with reference to the ocular system, noted that arsenicals with the amino group, or substituted amino group, in the para position to the arsenic produced lesions in the rabbit retina. It was their observation that if the amino group or its substitute group, were in the ortho or meta position to arsenic no lesion was produced in the optic nerve. Thus, it was suggested that the position of the amino group, or its substitute was of greater significance with relation to the production

70 King, O. H. Eye Contraindications to Arsenical Treatment of Syphilis, *South M. J.* **20** 284, 1927.

71 Smith, E. R. Tryparsamide in Neurosyphilis, *J. Indiana M. A.* **18** 125, 1925.

72 Casten, V. Tryparsamide Amblyopia Treated by Forced Drainage of Cerebrospinal Fluid, *New England J. Med.* **202** 676, 1930.

73 Fine, M., in discussion on Leinfelder⁸⁰.

74 Weeks, J. E., in discussion on Leinfelder⁸⁰.

75 Sharpe, O. A., in discussion on Leinfelder⁸⁰.

76 Muncy, W. M. Relationship of Tryparsamide Reaction to Vitamin Deficiency, *Tr. Am. Acad. Ophth.* **44** 134, 1939.

77 Leinfelder, P. J. and Stump, R. B. Thiamine Hydrochloride in Treatment of Tryparsamide Amblyopia, *Arch. Ophth.* **26** 613 (Oct.) 1941.

78 Young, A. G., and Loevenhart, A. S. Relation of Chemical Constitution of Certain Organic Arsenical Compounds to Their Action on the Optic Tract, *J. Pharmacol. & Exper. Therap.* **23** 107, 1924.

of ocular damage than was the valence of the arsenic. The dose of tryparsamide used in their experiments was comparatively larger than that used clinically.

The possibility of systemic retention of tryparsamide after injection, with cumulative toxic action, is in part answered by the studies of Young and Muehlberger⁷⁹, 3 of 4 patients observed excreted 88 to 95 per cent of the drug unchanged in the urine during the first twenty-four hours after injection. It was concluded that certain persons may show a slower excretion rate, this possibly increasing the likelihood of ocular reaction. Leinfelder⁸⁰ has commented that disintegration of pentavalent arsenicals which remain in the blood stream is very slow. Osborne⁸¹ has experimentally shown that arsenic can be identified in the brain of rabbits after therapeutic doses of tryparsamide, but Leinfelder has noted that neither arsenic nor the aniline group will cause the tryparsamide type of field defect characterized by peripheral contraction. Whether or not arsenic derived from tryparsamide reaches the cerebrospinal fluid has been considered.

A histopathologic study of the retina and optic nerves and tracts has been presented by Leinfelder⁸⁰. After an intravenous dose of 1 Gm of tryparsamide vision decreased from normal to amblyopia in each eye, death occurred from uremia nine days later. Prior to death a moderate degree of optic nerve atrophy had been noted, this was represented in the postmortem specimens as a slight gliosis without inflammatory or acute degenerative change. The nerve sheaths were normal. In the retina gliosis of the nerve head was correlated with the preexisting optic nerve atrophy. In the central portion of the retina areas of degenerative change were noted in the inner nuclear layer, cellular and nuclear structure could not be delineated. In the peripheral portion of the retina, where the greatest change was noted, ganglion cells had a cloudy or foamy cytoplasmic appearance, Nissl substance had largely disappeared, and nuclei were mostly destroyed. The nuclear degeneration and loss of Nissl substance were compared by Leinfelder to the marked cellular reaction occurring in acute intoxications of the central nervous system. A corresponding acute degenerative process was not noted in the optic nerves or tracts or in the lateral geniculate bodies, it was considered that the primary occurrence was a degeneration of the ganglion cells of the retina with secondary degeneration of both nerve fibers and myelin sheaths. With reference to this case, Leinfelder was able to comment that at least the factors of arteriosclerosis and alcoholism were not present and to conclude that ocular reactions following tryparsamide therapy are most likely of the nature of idiosyncrasy to the drug, a view supported by Cordes in a discussion of Leinfelder's case and by Woods and Moore.⁴⁷

In a similar study, Lazar⁶⁸ concluded that the histopathologic changes of a patient blinded three years before death by tryparsamide were those of syphilis rather than the result of the use of tryparsamide.

Sezary and de Font-Reaulx⁸² stated the belief that ocular damage is due to toxic action of the drug on the optic nerve rather than to reactivation of a latent lesion of the disease itself, a view which they stated was substantiated by studies which show degeneration rather than inflammation, their observation on patients

79 Young, A. G., and Muehlberger, C. W. Excretion of Tryparsamide, *J. Pharmacol. & Exper. Therap.* **23** 461, 1924.

80 Leinfelder, P. J. Pathologic Changes in Amblyopia Following Tryparsamide Therapy, *I. A. M. A* **111** 1276 (Oct. 1) 1938.

81 Osborne, E. D., Putnam, E. D., and Hitchcock, B. S. Effect of Arsenic on Rabbits, *Arch. Dermat. & Syph.* **25** 419 (March) 1932.

82 Sezary, A., and de Font-Reaulx, P. La neurite optique de l'arsenic pentavalent, *Ann. de dermat. et syph.* **4** 289, 1933, cited by Sloan and Woods.⁷²

with optic nerve atrophy treated with sodium arsenite and tryparsamide who had neither syphilis nor trypanosomiasis, and finally, the experimental evidence that these ocular changes can be reproduced in animals by giving them pentavalent arsenicals. The fact that ocular complications occur with greater frequency in patients with involvement of the nervous system and may occur after only a few injections has been advanced as an argument in favor of reactivation of the lesion. Sézary and de Font-Réaulx suggested that a preexisting lesion may render nerve fibers more liable to injury by the toxic action of the pentavalent drug.

Apparent activation of a syphilitic process by tryparsamide with deleterious effects on the optic nerve was described by Lillie⁸³ when he reported a case of tabes dorsalis in which the vision and visual fields were normal prior to anti-syphilitic therapy. Arspenamine, sulfarsphenamine and tryparsamide were administered. A contraction of the fields described as slitlike occurred, this apparently was not related to any specific drug. Diffuse degeneration of the nerves, more pronounced in the periphery, was noted at necropsy, at which time a pathologic diagnosis of perineuritis was made.

LEGAL ASPECTS OF TRYPARSAMIDE THERAPY

The important legal aspects of the uncontrolled (ophthalmologically) administration of tryparsamide associated with detrimental visual sequelae are well exemplified by the following court action (Reed versus Church⁸³). During a period of fourteen years following initial treatment of cerebrospinal syphilis in 1923 a plaintiff enjoyed good health. His eyesight was good although a pair of glasses was purchased in 1930. In 1937 this plaintiff fainted suddenly and on reexamination was noted to have violent headache and incoherence of speech. The defendant physician certified at this time that the patient was suffering from severe hypertension. Despite this diagnosis and a negative Wassermann reaction of the blood, the defendant physician concluded that the plaintiff had a recurrence of cerebrospinal syphilis and commenced to administer a series of injections of tryparsamide. This drug, an arsenic compound, was sold in ampules around each of which was a pamphlet advising, among other things, that treatment be discontinued immediately on the appearance of any ocular disturbance. After, or at the time of, the third injection the plaintiff complained that the injections were making his eyes a little blurry, but each time he complained the defendant physician advised him that his difficulty would clear up. It did not, however, and the plaintiff subsequently became almost completely blind, with "central," or "gun barrel," vision due to permanent optic nerve atrophy. The plaintiff brought suit against the defendant physician for malpractice and obtained a judgment in his favor. The defendant physician then appealed to the Supreme Court of Appeals of Virginia. The plaintiff testified that after he had complained of having trouble with his eyes the defendant continued the tryparsamide treatment and gave him in all nine injections. The defendant maintained that there were two schools of medical opinion as to whether the use of tryparsamide should be continued after the discovery of ocular disturbances. The one theory reasoned that the continued use of the drug by helping the syphilis would help the optical disturbances, the other theory suggested that use of the drug be discontinued immediately on the complaint of visual trouble. The defendant therefore contended that if he followed either one of these theories

83 Malpractice—Liability of Physician for Blindness Caused by Administration of Tryparsamide [Reed vs Church], *Medicolegal Abstract*, report of the Bureau of Legal Medicine and Legislation, J A M A 116 891 (March 1) 1941

he had not been negligent. The court held that the defendant's testimony "that he stopped giving the injections after the plaintiff complained about his vision" committed him to the second school of medical opinion. However, since his testimony in that regard was disputed by the plaintiff, it was the opinion of the court that the important question for the jury's determination did not relate to the rule that when there are two schools of thought in medical practice if the physician follows one he cannot be negligent, but did relate to whether or not the defendant properly and carefully followed the branch of medical opinion which he had adopted. On this point the jury resolved the question against him. A physician, continued the court, is liable only for a failure to possess and exercise that degree of care and skill ordinarily exercised by prudent practitioners in his community. In the present case, therefore, the plaintiff was required to show that his blindness was caused not by the cerebrospinal syphilis but by the injections of tryparsamide and that those injections were given in contravention of good practice in that community. If it were equally probable that the blindness was caused by either, the plaintiff could not recover. Evidence showed that it is well known in medical circles that either the cerebrospinal syphilis or the injections of tryparsamide could cause serious ocular trouble. Two physicians did testify that in their opinion the atrophy of the plaintiff's optic nerve was of syphilitic origin, but they admitted that it was impossible to determine by examination whether this was due to syphilis or to arsenical poisoning. It would appear that no amount of clinical research could determine which of the forces here at work caused the atrophy, so it was for the jury to waive the probability and decide. The jury did so and found, which finding in the opinion of the court was justified by the evidence, that it was not equally probable that syphilis caused the ocular trouble, but rather that the defendant's treatment was the proximate cause of optic nerve atrophy. The evidence showed that for fourteen years after being treated for syphilis the plaintiff had had no ocular trouble, that in 1937, despite a negative Wassermann reaction, the defendant treated him for syphilis with tryparsamide, a potent drug which should be administered only under ocular control, which the defendant failed to exercise, that in spite of the plaintiff's complaint of increasing visual disturbances the defendant continued the injections of the drug, and that more than a year later the plaintiff underwent an extensive examination for the presence of syphilis which proved to give negative results, although the blindness remained. Because there was evidence, though conflicting, that at the time the plaintiff fainted on Aug. 14, 1937 he had a headache, an elevation of blood pressure and incoherence of speech, and in view of his age of almost 62 years, the oppressive heat at the time and the negative Wassermann reaction, the court was of the opinion that there was evidence from which the jury might have concluded that there was not sufficient proof of the recurrence of syphilis to justify the defendant in administering tryparsamide in an uncontrolled manner. In fact, there was medical testimony that such treatment, persistently administered despite increasing loss of vision, may be proper only in the case of an extremely aggravated syphilitic condition, and there was evidence that in the present case no such condition existed. The court, therefore, refused to disturb the jury's verdict and affirmed the judgment for the plaintiff.

SUMMARY

It is manifest according to material accessible to review that a precise evaluation of the various factors that contribute to impairment of vision during therapy with tryparsamide is not to be derived from the literature on the subject. In the introduction to this review the factors operating to veil the entire subject in factual

obscurity were elucidated. Such analytic data as may be reasonably derived are approximately as follows:

There is noted no indication that sex, race or age of the patient is related to untoward visual effect during therapy with tryparsamide. This generalization must allow, however, for two possible discrepancies. Neurosyphilis usually and tabes dorsalis certainly are disease processes of the middle decades of life, the use of tryparsamide exclusively for these conditions suggests that factual data based on investigational material for other age groups would not be available and that statistics regarding this subject would not be applicable to the earlier or later decades of life. It has been noted that reports pertinent to the visual effects of tryparsamide therapy appearing in the foreign literature have shown both a higher and a lower incidence of unfavorable visual involvement than has been noted in the recent domestic literature. The fact that tryparsamide was first available in this country would suggest that the recent discrepancies of the foreign literature are comparable to the confusion indicated in American literature during the first years after the clinical introduction of the drug into this country. With reference to sex and race, no data of considered significance were obtained.

The dose of the individual injection, the number of injections and the length and number of courses of injections have not been noted to be associated with visual effects in a consistent manner. On one occasion the comment was made that "smaller doses tended to be more productive of unfavorable (visual) results." In the absence of verification of this observation, it is not possible to offer the conclusion that the amount of the individual dose explains the visual reaction. The number of doses of tryparsamide has long been a factor acknowledged to be associated with visual deterioration. It is generally considered that if untoward effects are to occur, these will be noted prior to the tenth injection. Evidence of such a belief is current throughout the literature. Statistically, however, such a presupposition is apparently poorly borne out, and in the light of the figures presented, which are the most complete available on this particular phase of the subject (Downs⁵⁰), the opinion is best modified to state that most reactions, especially "acute" ones, are noted relatively early in the series of tryparsamide injections, but such a statement must not preclude recognition that deleterious effects may occur later in the period of treatment.

With regard to the character of the reaction which occurs during a series of tryparsamide injections the classification of Sloan and Woods is of assistance. Types of visual effects are designated by them as acute and chronic, with the latter type subdivided into objective and subjective. The chronic subjective reaction is characterized as occurring in approximately 5 to 10 per cent of patients receiving tryparsamide therapy and consists of flashes, sparks or spots before the eyes, together with visual distortions and slightly decreased central visual acuity. Objective findings are not usually detected, the prognosis is good if therapy is discontinued.

With regard to the subjective type of reaction, patients frequently have visual complaints based primarily on their apprehension, many patients are prone to answer in the affirmative regarding visual phenomena, and close interrogation with regard to the exact character of such occurrences is desirable before a decision to discontinue use of the drug is made.

Objective chronic reactions are specified to occur in a smaller number of patients (4 to 5 per cent) receiving tryparsamide therapy, with permanent unfavorable results in about 1 per cent. This type of reaction consists of contraction of the visual field, involving primarily the upper and lower nasal areas, with relative

sparing of the temporal portions. Moderate depression of central vision is frequently noted, central scotomas and enlargement of the blindspot are not characteristic of this type of reaction. The prognosis regarding restoration of vision is held to be good if the condition is recognized and the drug withdrawn promptly. There is sufficient evidence that after an initial visual reaction the deleterious effect will recur on resumption of tryparsamide therapy to render it advisable to withdraw the drug permanently once an untoward effect of either an objective or a subjective character is noted.

During routine administration an initial expansion of the fields with later moderate contraction of the peripheral field has been described as a usual occurrence. It is possibly incorrect to refer to such minimal contraction as a reaction, although it is reasonably inferred that such an occurrence must, nevertheless, be of the nature of a reaction.

Acute reactions are distinct from chronic reactions in all characteristics, including, possibly, even causation. The percentage incidence of such reactions to tryparsamide therapy is not disclosed in a review of the literature, certainly, however, they are much more infrequent than chronic ones. Usually occurring prior to the fifth injection of the drug, they are characterized by rapid deterioration of both central and peripheral vision. Complete details in a sufficient number of cases are not available in the literature to indicate in a satisfactory manner the actual outcome of the original visual deterioration. Such cases as are deemed eligible in a statistical consideration of the prognosis of such reactions indicate that in approximately one half permanent visual loss will obtain, while in the other half relatively complete restoration of vision may occur.

The foremost question with regard to the use of tryparsamide has revolved around the question of atrophy of the optic nerve and the suspected effect of the drug when this condition is noted prior to the initiation of tryparsamide therapy. It is permissible to state that opinion in regard to this matter as reflected in the literature is approximately equally divided among physicians who when primary syphilitic optic nerve atrophy is present would withhold the drug and those who under similar conditions would favor its use. Any preponderance of opinion evaluated in terms of the evidence presented would incline to the view that detectable syphilitic involvement of the visual tracts offers some type of predisposition or possibly sensitization to the drug, but there is lacking indication that the presence of optic nerve atrophy actually establishes a satisfactory contraindication to use of the drug. When optic nerve atrophy is present possible arbitration of the problem is best accomplished by closer surveillance of the patient before and during tryparsamide therapy than would otherwise be offered, with immediate and permanent withdrawal of the drug if tangible evidence is obtained that the drug is actually contributing to the further deterioration of vision. The consensus is complete that remissions of the process of primary syphilitic optic nerve atrophy, together with recurrences of the process, are common to *tabes dorsalis* and such conditions must not be confused with a suspected effect of tryparsamide therapy. In view of the hopeless course of primary syphilitic optic nerve atrophy when untreated, and the fact that other treatment (with the exception of fever therapy), offers little or no hope of arresting the process, and in recognition also that beneficial action may be received from the use of tryparsamide to the same extent that deleterious effects may occur, it seems inadvisable to permit the establishment of any rule as such to govern therapy with tryparsamide or withholding of the drug.

That the differential diagnosis between the normal condition of the optic disk and that of primary syphilitic optic nerve atrophy is not always clearcut is attested by the fact that the color of the disk, the visual acuity and the visual field findings may yield contradictory evidence. With the introduction of the numerous complex factors associated with visual impairment during treatment with tryparsamide, confusion as to the probable cause of visual impairment is present. Of the various examinations available, apparently the examination of the visual fields offers the most thorough information in regard to the exact nature of impairment of vision. The visual field defects of optic nerve atrophy are described as concentric peripheral contraction, localized defects in the peripheral fields and central or cecocentral scotomas. The peripheral contraction is moderate and affects especially the nasal portion, usually with sparing of central vision.

The intimate or exact nature of the reaction to tryparsamide remains obscure in the literature. Repeatedly suggested to explain visual involvement are a hypothetical toxic effect of the drug on the nerve or retina, idiosyncrasy to the drug, factors superimposed by drug therapy on active syphilitic involvement (reactivation of a process) and the Jarisch-Herxheimer reaction. Factors such as the valence of the arsenic in the preparation, the structure of the tryparsamide molecule and the factors of retention-excretion and metabolism have been considered without the establishment of a conclusive opinion concerning the mechanisms of the reaction.

The relatively infrequent occurrence of systemic effects is against any theory holding tryparsamide to be a toxic drug generally, contrarily, the type of visual impairment is suggestive of a toxic effect in the nature of an idiosyncrasy, especially in the acute reactions. There is an absence of proof that syphilis or any other condition predisposes to a reaction to tryparsamide. There is, however, the implication that the exact mechanism of the acute and of the chronic type of reaction may be different. In the light of the clinical and pathologic material available in the literature, other factors functioning to produce visual involvement cannot be adequately evaluated. There is no indication that the use of the drug should be condemned, contrarily, therapy is fully desirable, but closer observation ophthalmologically of patients, certainly during the preliminary stages of therapy, seems the most desirable conclusion of the clinical aspects of the problem.

News and Notes

EDITED BY DR W L BENEDICT

SPECIAL NEWS

A dinner in honor of Dr Walter B Lancaster was given on October 14 at the Coronado Hotel, St Louis, by the St Louis Society for the Blind in cooperation with the National Society for the Prevention of Blindness and the Association for Research in Ophthalmology. The dinner was given on the occasion of the award of the Leslie Dana Medal for the Prevention of Blindness.

SOCIETY NEWS

Canadian Ophthalmological Society—The sixth annual meeting of the Canadian Ophthalmological Society was held at Toronto, Canada, Sept 24 and 25 1943.

The following papers were presented:

‘Color Photography of External Disease’ A Lloyd Morgan, M D, Toronto
‘Corneal-Scleral Suture,’ R J P McCulloch, M D, Toronto, ‘Sulfonamide Compounds in Local Ocular Conditions,’ Alson E Braley, M D (by invitation), New York, ‘Mixed Cell Tumors of the Lacrimal Glands,’ J A MacMillan, M D, Montreal ‘Ophthalmologic Research in the Royal Canadian Navy,’ Surgeon Commander C H Best and Surgeon Lieutenant Commander Donald Y Solandt Toronto, ‘Orthoptics in Aviation,’ Squadron Leader J V V Nicholls, M D, Montreal, ‘Orbital Implants,’ W W Wright, M D, Toronto, ‘Xerophthalmosis and Circumcorneal Congestion in the Navy,’ Surgeon Commander E A Amos R C N V R, ‘Retinal Arterial Tension in Epilepsy,’ G A Stuart Ramsay, M D, Montreal, ‘Hereditary Disease of the Eye,’ Madge T Macklin, M D, London, Ontario, ‘Amaurosis Caused by Blastocytoma of Adrenal,’ Colin Campbell, M D, Toronto, ‘Colored Moving Pictures of Eye Operations,’ Major J P Gilhooly, R C A M C Ottawa, Ontario

Asociación para evitar la ceguera en México—Dr William Thornwall Davis was invited to read a paper on Aug 17, 1943 before the Asociación para evitar la ceguera en México (Society for the Prevention of Blindness in Mexico) on amblyopia ex anopsia. Since he was unable to deliver the paper personally, the department of ophthalmology of the George Washington University School of Medicine made a sound film of the paper in Spanish, which was sent by mail to Mexico and produced at the meeting of the association on the date appointed. Dr Davis read the introductory paragraphs of the paper, and Dr Castillo Najera, of the George Washington University School of Medicine, 1942, read the main body of the paper for Dr Davis.

UNIVERSITY NEWS

Ophthalmologic Research at the University of Oxford—An announcement in *Science* (98:318 [Oct 8] 1943) states:

The University of Oxford is planning the establishment of a department for ophthalmological research, the activities of which would include research, teaching and the treatment of patients. The Ophthalmological Research Endowment Committee is asking for help in raising £250,000 to build, equip and endow the research laboratories of a department of ophthalmology at the university. Contributions received during the war will be invested in Government securities. The treasurer of the Ophthalmological Research Endowment Fund, Old Clarendon Building,

Oxford, will receive contributions. Expenses of the appeal are being met by the generosity of the National Institute for the Blind. *The Times*, London, reports that

“The facilities available for such work are considered wholly inadequate, and the university is appealing for funds towards the establishment of research premises in connection with the Oxford Eye Hospital, the rebuilding of which will be begun at the end of the war, the provision of salaries for full-time and part-time research workers, teachers and technicians engaged in the new department, and the defraying of the working costs of researches which would have for their aim the prevention of blindness, the improved treatment of eye disease and the promotion of a higher standard of visual function throughout the country

“Under the proposed regional scheme of the Joint Hospitals Board, the Oxford Eye Hospital will become the chief regional center (covering the counties of Oxford, Buckingham and Berkshire) for ophthalmological work and teaching. For this the present hospital is inadequate, and is to be rebuilt, the necessary funds being raised by a separate appeal from local sources

“One of the problems which the proposed department at Oxford would examine would be that of discovering the safest anti-bacterial drugs for ophthalmological purposes. The extreme delicacy of the eye is the governing consideration, as all the usual antiseptics are poisons, and further investigation will need contributions not only from ophthalmology, but bacteriology, mycology and chemistry. The most promising substance found so far is penicillin, the development of which is largely the result of work done in an Oxford laboratory

“The Oxford scheme, which will be generally welcomed, will form an important contribution towards the great national effort that is being made to abate the toll and suffering and economic wastage due to loss of sight and defective vision. Statistics prove that, while failure of vision is a hazard common to all, the risk falls increasingly on those who are in middle and later life. In 1941 out of a total blind population of 74,000 in England and Wales 63,000 were persons over 40 years old.”

Obituaries

GEORGE HUSTON BELL, M D

1866-1943

Dr George Huston Bell was born in Mount Sidney, Va, on Aug 10, 1866, one year after the close of the Civil War. He died suddenly in New York on Oct 5, 1943. His father before him, Dr William Bell, was a physician. He came of English and Scotch ancestry, long established in the Valley of Virginia. He received his early education at the Augusta Military Academy, Fort Defiance, Va, one of the best known preparatory schools for boys in the South. He obtained his degree of Doctor of Medicine from the University of Virginia in 1897. Immediately thereafter he entered on his long career in ophthalmology. In 1899 he completed his internship at the New York Eye and Ear Infirmary. His connection with this institution spanned a period of forty-five years, interrupted only once, in early life, by a year spent in postgraduate work in Europe. In 1917 he was appointed a full surgeon at the Infirmary, with a clinic of his own, Dr Conrad Berens serving as his chief of clinic. Twelve years later, in 1929, he became consulting surgeon, which appointment he held until his death.

Although Dr Bell's surgical activities were centered at the Infirmary, he found time to serve also on the staffs of other institutions, including the United States Marine Hospital on Staten Island, N Y, the Hudson Street Hospital, the St Andrew's Convalescent Hospital and the New York Polyclinic Medical School and Hospital, in which he was professor of ophthalmic surgery.

Most of Dr Bell's contributions to the literature reflected the trend of thought of American ophthalmology in the early years of the present century. Thus, in his best known papers he discussed the teeth, the tonsils and toxemia, the "three T's" as he termed them, in their relation to diseases of the eye. He established the procedure against postoperative infection, now in use at the Infirmary, namely, the instillation of a 1 per cent solution of silver nitrate into the conjunctival sac an hour before the time set for operation. In a paper published in 1926 he was able to report on 1,500 major ophthalmic operations without a single infection. Toward the end of his surgical practice, when nearing the age of 70, he estimated that he had performed 3,000 cataract extractions.

He was a fellow of the American College of Surgeons, a member of the American Ophthalmological Society, a member of the New York Ophthalmological Society and a member of the New York Academy of Medicine.

Dr Bell possessed a kindly, generous nature and retained to the last a high flow of spirits. He was an active member of the Virginia Society and the Southern Society in New York. In him the homing instinct was well developed. He maintained the old homestead, "Bellview Farm," near Mount Sidney, Va, where he passed his summer vacations. His clubs were the Ardsley Country Club and the Racket and Tennis Club. He belonged to the Phi Kappa Psi Fraternity. He was a Mason and a Presbyterian. In singular ways his life paralleled that of the late Dr Robert G Reese. They were born in the same year and were brought

up in the same county, their fathers had been surgeons in the Confederate Army, they attended the same schools, they both graduated in pharmacy before studying medicine, they belonged to the same fraternities, they interned at the same institution, and they both enjoyed a lucrative practice. No surgeons ever served the New York Eye and Ear Infirmary more faithfully and devotedly than these two men, and few over a longer period.



GEORGE HUSTON BELL, M.D.
1866-1943

Dr. Bell's death, at an advanced age, brought to an end a happy life, eminently successful in every way. He will be missed by many friends and patients. Surviving him are his widow, Mrs. Florence Winifred Collins Bell, a brother, Archibald H. Bell, of Richmond, Va., and three sisters, Mrs. Clifford Piater, of Knoxville, Tenn., Mrs. John Cyrus McCue, of Fort Defiance, Va., and Miss Willie Bell, of Mount Sidney, Va.

BERNARD SAMUELS

Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

Cornea and Sclera

TREATMENT OF EPIDEMIC KERATOCONJUNCTIVITIS A E BRADLEY and M SANDERS, J A M A 121 999 (March 27) 1943

The authors discuss 10 cases of epidemic conjunctivitis in which there were the following manifestations pronounced edema of the lids, conjunctiva and semilunar fold, with bulbar chemosis, involvement of the preauricular lymph nodes, usually both the submental and the anterior cervical, severe ocular discomfort associated with excessive tearing, appearance in conjunctival scrapings of mononuclear cells with practically no polymorphonuclear leukocytes, and negative cultures

In 9 of the cases striking clinical improvement occurred a short time after intravenous injections of human convalescent serum were given. However, need for a controlled group of cases cannot be stressed too strongly. It has been pointed out that there is no correlation between the intensity of the clinical symptoms and the duration of the disease. It should also be remembered that it is highly desirable that the present study be enlarged from the point of view both of cases in which there is treatment and of control cases, and that standard, accurately titrated convalescent serums be employed

W ZENTMAYER

ACNE ROSACEA KERATITIS AND RIBOFLAVINE (VITAMIN B₂) W M FISH, Brit J Ophth 27 107 (March) 1943

The author quotes from the literature to the effect that "rosacea keratitis (so-called) may be the direct result of deficiency of riboflavin" and further that "the term 'dietary keratitis' (used by Sydenstricker) appears to indicate a new designation of the condition familiar to ophthalmologists as rosacea keratitis, so-called." Fish considers this rather surprising in view of the fact that acne rosacea is a rare disease in the southern states of America, where riboflavin deficiency is common, and is not even mentioned in Sydenstricker's paper.

The author studied 45 patients with acne rosacea with the slit lamp in order to find out whether they showed the type of corneal vascularization demonstrated to him by Sydenstricker as diagnostic of ariboflavinosis, e g, a bilateral, symmetric superficial proliferation of new streamer-like fine vessels from the limbal loops, forming a more or less regular pattern all around the cornea and extending toward its center. Of these 45 patients all had the cutaneous and all but 2 the corneal lesions typical of rosacea, but only 3 had the bilateral corneal involvement, so that in 40 cases there was a control eye, unaffected by ulceration, in which to look for the corneal vascularization typical of ariboflavinosis, which, though not always equal in the two eyes, is always bilateral. This type of vascularization was absent in all 40 cases.

In the present series rosacea keratitis does not appear to be the direct result of ariboflavinosis.

W ZENTMAYER

General

COLOUR IN PROTECTIVE NIGHT LIGHT C E FERREE and G RAND, Brit J Ophth 27 173 (April) 1943

Ferree and Rand state that in the selection of a color for protective night light, the ocular factors as well as power to penetrate the external atmosphere, should be taken into consideration—namely, the comparative sensitivity of the eye to colored light at very low intensities, visual acuity at low intensity and adaptation

factor is. An instrument termed a variable illuminator has been made in the form of a lamp with the opening turned downward or obliquely downward. By means of a rotatable shutter the light can be varied in continuous change from full to extinction, so that it can be used as a night light to obtain a complete black-out or as near a complete black-out as may be desired. In this lamp any color, type or wattage of bulb can be used, even the small neon night bulb. Suitably equipped, it should serve a useful purpose in protection night lighting, even when total extinction of light for a complete black-out is necessary. W ZENTMAYER

Hygiene, Sociology, Education and History

OPHTHALMOLOGY AND SOCIOLOGY. A LOEWENSTEIN, Bull Czechoslovak M A in Great Britain, 1942, no 3

After discussing the main causes of blindness, the author suggests means of prevention. It is difficult to prevent hereditary disease or defects, and he suggests that advisory offices might be established where engaged couples could get guidance. Statistics have shown that blindness from venereal disease is rapidly decreasing. Antepartum treatment is now well established and is distinctly successful. The greatest modern problem is injuries in the industrial countries. Many injuries in workshops are due to defective illumination, the author states that at least 15 per cent of all injuries to the eyes are caused by insufficient lighting. In one factory after modern lighting fixtures were installed, the frequency of accidents was reduced by 7 per cent. Also, industrial efficiency depends on good vision. It is necessary to control toxic materials, such as gases, dusts and vapors, to provide protective goggles against flying objects and radiant energy, and to provide adequate illumination. In the final section the author stresses the need of more careful teaching of ophthalmology in the medical schools. This would result in a great stock of good ophthalmic surgeons to carry on the battle for the sight of the rising generation.

ARNOLD KNAPP

Methods of Examination

NEUTRALIZING CYLINDER GLASSES AS TEST FOR MALINGERING. H. LYTTON, Brit J Ophth 26: 512 (Nov) 1942

Malingering by claiming a reduction in visual acuity to approximately the same extent in the two eyes is difficult to unmask.

Lytton has found the following test useful. In addition to the glass which gives the best possible correction, a plus cylinder glass, e. g., +1.00 D cyl, axis 90, is put in the rear immobile groove of the trial frame, and the corresponding minus glass, —1.0 D cyl, axis 45, is placed in the revolving compartment in front. Now the examinee is asked to change the axis of the minus cylinder by revolving it until he obtains the clearest definition of the test types. It speaks strongly for his honesty if he turns the axis into the neutralizing position of 90 degrees. A malingerer is likely to put the axis at 180 degrees. If he still claims to see, for instance, the fourth line of the chart, indicating a visual acuity of 6/18, it is proved that his vision is at least 6/9, as the crossed cylinder reduces the visual acuity about 50 per cent.

W ZENTMAYER

Neurology

STUDIES ON THE CORPUS CALLOSUM. V. HOMONYMOUS DEFECTS FOR COLOR, OBJECT AND LETTER RECOGNITION (HOMONYMOUS HEMIAMBLYOPIA) BEFORE AND AFTER SECTION OF THE CORPUS CALLOSUM. A. J. AKELAITIS, Arch Neurol & Psychiat 48: 108 (July) 1942

Three cases are reported in which routine perimetric fields were normal but homonymous hemiamblyopia was present. The methods of testing are described in detail. Briefly, the authors found gross studies more reliable and informative

than the use of small test objects on the Bjerrum screen. Such studies included appreciation of various shades of gray as utilized in Hering's gray paper series, appreciation of form by use of geometric figures as found in the Stanford-Binet series and attentiveness to two similar objects presented simultaneously to identical points in each homonymous field. Each patient showed loss of recognition of forms, objects and letters and impairment of attentiveness and of perception of illumination. The usual remark was, "I see something but don't know what it is."

Evidence in each of the cases suggested that the hemiamblyopia resulted from a lesion in the posterior portion of the contralateral hemisphere. However, the author points out that cases have been reported in which lesions of the optic tract were responsible, and he therefore concludes that hemiamblyopia has only limited localization value.

Complete or partial section of the corpus callosum produces no changes in the hemiamblyopic visual field.

R IRVINE

BOECK'S DISEASE (SARCOID) OF THE CENTRAL NERVOUS SYSTEM. REPORT OF A CASE, WITH COMPLETE CLINICAL AND PATHOLOGIC STUDY. T. C. ERICKSON, G. ODOM and K. STERN, *Arch Neurol & Psychiat* 48: 613 (Oct) 1942.

A case is reported with complete clinical and pathologic study, showing a clinical picture of adhesive arachnoiditis with internal hydrocephalus. There was progressive bilateral papilledema with retinal hemorrhages and visual loss.

Biopsy of a nodular lesion from the upper lip established a diagnosis of Boeck's sarcoid, and examination of granulomatous processes within the central nervous system resulted in a similar diagnosis.

R IRVINE

HISTOGENESIS OF THE EARLY LESIONS OF MULTIPLE SCLEROSIS. I. SIGNIFICANCE OF VASCULAR CHANGES. M. SCHEINKER, *Arch Neurol & Psychiat* 49: 178 (Feb) 1943.

The author provides the following summary:

"In 20 cases of multiple sclerosis the early stages of plaque formation and their relation to the vascular system were studied. A positive correlation was found between the early lesion and the presence of vascular abnormality. The view is expressed that vascular change, particularly occlusion by thrombosis, is an essential factor in the pathogenesis of demyelinated plaques."

R IRVINE

Ocular Muscles

ANOMALOUS RETINAL CORRESPONDENCE. D. E. DICKE, *Am J Ophth* 25: 585 (May) 1942.

Dicke reviews the frequency and manner of development of anomalous retinal correspondence and discusses the tests for its presence. She emphasizes the value of preoperative treatment of patients who will be subjected to surgical intervention.

W. S. REESE

ORTHOPTIC TREATMENT OF ANOMALOUS PROJECTION. D. S. MANN, *Brit J Ophth* 27: 215 (May) 1943.

As indicated by the title of the article, Mann prefers Verhoeff's term—*anomalous projection*—of the many under which the phenomenon goes. Details of the preoperative treatment are given. Operation is almost inevitably necessary, and there is no point in prolonging treatment before operation if the patient shows no improvement after three or four visits. The only general prerequisites are that the vision should be equal and the patient should be able to alternate readily. When the

operative result is good, the probability is that some binocular vision may be recovered in time without orthoptic treatment. However, the recovery is seldom complete, and in general the postoperative treatment is essentially the same as the preoperative.

W ZENTMAYER

The Pupil

ANOMALOUS PUPIL REACTIONS B G EDELSTON, Brit J Ophth 26: 507 (Nov) 1942

Three cases of anomalous pupillary reactions are reported. The first patient was a man aged 30 with tabes dorsalis. The pupils were small, equal and centrally placed. They dilated to an appreciable degree to light. There was early optic nerve atrophy. The Wassermann reaction was strongly positive. The second patient was a man aged 59. There was a history of a primary sore at the age of 29. The pupils were moderate in size, centrally placed and equal. Light stimulus caused a moderate dilatation. The Wassermann reaction was strongly positive. At autopsy a new pulmonary growth in a caseous condition was found. The third patient was a woman aged 28. The left pupil was larger than the right and was immobile to light but showed slight slow contraction in convergence. All the superficial reflexes except the biceps jerk were absent. The patient was normal in every other respect. Although when she was 10 years old a diagnosis of juvenile tabes was made, Edelston believes the pupillary phenomenon to be an example of myotonic pupil.

W ZENTMAYER

Refraction and Accommodation

MUSCLE BALANCE IN MYOPIA W W BAUM, Am J Ophth 25: 291 (March) 1942

In this rather brief article Baum concludes from his studies of muscle balance in myopia that orthoptic treatment is of definite value in the control of the common functional myopia seen in children and young adults.

W S REESE

THE PROBLEM OF THE HYPERMETROPIC MINER A C REID, Brit J Ophth 27: 110 (March) 1943

Reid points out that the myopic miner who consistently wears his correction on top can dispense with glasses below ground. This is not true of the miner with high hypermetropia, who has to accommodate to see his work, since a miner's work is done mostly within arm's length. Fourteen cases of hyperopia of high degrees are recorded to show the points the author wishes to raise. Seven of the patients who had an error of between 2 and 4 in the lowest axis averaged 37 years of age, the extremes being 28 and 44. With a +4 D error few men can go beyond the age of 30 at the coal face. With an error of +6 D or more, probably no man should go below, and few do. It would therefore seem reasonable to advise lads with both eyes good not to go down if the error is +3 D or more and squinters or amblyopes not to go down at all. Much can be done in advising the parents when a boy is about to leave school.

W ZENTMAYER

Retina and Optic Nerve

NOTE ON SOME SYMPTOMS ASSOCIATED WITH A RETINAL LESION E G HILL, Brit J Ophth 27: 97 (March) 1943

At the age of 47 the author experienced some difficulty in vision accompanied by the appearance of a veiling patch of light. Corrected vision in each eye was 6/5. No scotoma was present. Ophthalmoscopic examination by Williamson-Noble disclosed in the right eye a shimmering area in the macular region which

the examiner attributed to some thickening of the internal limiting membrane of the retina. The fundus of the left eye was normal. The symptoms noted by the patient were image distortion with localized aniseikonia, the appearance of a luminous or a shadowy veil, a phenomenon termed the "after flash," convergence effect and pain. The author gives a detailed description of the symptoms and suggests the following explanation:

"The image distortion may presumably be attributed to a displacement of the retinal elements, and the character of the change shows that the centre of the retina must be bunched. The convergence effect seems to indicate a residual lack of rigidity in the posterior structure of the eye. It may also be mentioned here that, associated with these changes, a blind patch of ten minutes subtense made its appearance and is located, presumably significantly, exactly at the centre of the fovea.

"The flash and veil phenomena are presumably bound up with the bleaching of the visual purple, and it would seem that the lesion has disturbed this mechanism over the affected area. As there is no reduction in the level of dark adaptation, the failure seems more related to the actual bleaching reaction than to the secretion of visual purple. The discrimination between the effects in blue and other colours may contribute to the elucidation of the mechanism of dark adaptation, as there is reason to suppose that the rate of dark adaptation is a function of the colour of the preadapting light."

The article is illustrated

W. ZENTMAYER

ON SOME ANOMALOUS FORMS OF AMAUROTIC IDIOCY AND THEIR BEARING ON THE RELATIONSHIP OF THE VARIOUS TYPES. R. WYBURN-MASON, *Brit J Ophth* 27: 145 (April), 193 (May) 1943

Wyburn-Mason reports a group of cases of amaurotic idiocy of the type described by Tay, in some of which there were atypical features. This is followed by a group of cases of the juvenile type, in some of these the disease was of the late infantile type described by Bielschowsky under the term "late infantile familial amaurotic idiocy with cerebellar symptoms." Still another group comprises instances of the late juvenile type. Finally, an adult type is described.

Evidence is brought forward that there are two types of the disease, infantile and juvenile, which are not related to one another except in their similar histologic appearances. It is probable that atypical forms of the juvenile disease occur in which either the retinal or the cerebral manifestations are absent, especially in older patients. It seems likely that the disease is unrelated to macular heredodegeneration.

The article is illustrated with fundus drawings

W. ZENTMAYER

Trachoma

SULFANILAMIDE IN THE TREATMENT OF TRACHOMA. R. SORY, *Am J Ophth* 25: 713 (June) 1942

Sory presents the following summary and conclusions:

"1. In experiments for control, patients receiving sulfanilamide by mouth underwent treatment in one eye with drops of the drug, and in the other with either grattage or application of silver or copper salts, recovery from infection occurred only in the latter eye.

"2. Of 49 patients treated with sulfanilamide alone, the condition in 14 was unchanged, in 21 improved, and in 14 arrested, 7 of the cases being of the "flare-up" variety.

"3. The drug had least beneficial effect on papillary or follicular hypertrophy of the conjunctiva, its best effect was on the corneal lesion associated with the 'flare-up' type.

"4 In combined sulfanilamide and other treatment, an analysis of 274 patients reveals arrest in 235 (86 per cent), improvement in 38 (14 per cent), and no change in one

"5 In the combined therapy, grattage and chemical treatment were of approximately equal effectiveness, their selection should vary in different patients depending upon the character of the disease

"6 In operations performed to correct sequelae of trachoma, it is thought that sulfanilamide may also be of use

"7 The results of this study indicate (a) that sulfanilamide only exceptionally arrests trachoma, and by itself is less reliable than other accepted forms of treatment, (b) in conjunction with other therapeutic measures, recovery is accelerated, and a high degree of efficacy is readily attainable, (c) even in the latter instances recurrences may occur, suggesting that trachoma is, as formerly, *arrested* and not *cured*"

W S REESE

Uvea

PROGRESSIVE ATROPHY OF THE IRIS WITH FORMATION OF HOLES AND INCREASED INTRAOCULAR TENSION REPORT OF CASES J SCHARF, *Klin Monatsbl f Augenh* 106:411 (April) 1941

Two cases of progressive atrophy of the iris with formation of holes in the iris and increased intraocular tension are reported. The patients, both women, were 51 and 26. The result of gonioscopic examination is described and evaluated. As this disease is described by a number of writers quoted, great rarefaction of the stroma of the iris occurs with progressing formation of holes, the area of the sphincter remains intact the longest and glaucoma of a malignant type follows, resisting all local and surgical therapy. Usually only one eye is affected. Regarding the origin of glaucoma, no agreement was arrived at by a number of observers. Scharf found peripheral synechias causing adhesions between the root of the iris and the inner corneal surface at a time when no evidence of glaucoma could be obtained, not even by provoking tests. Furthermore, he does not accept the theory that accumulation of pigment and obliteration of the canal of Schlemm may be the cause of glaucoma, because considerable pigmentation of this area was observed in his second case in the absence of glaucoma.

In the author's opinion the disease described is due to developmental disturbances of the mesoderm of the anterior segment of the eyeball. The uveal fetal tissue, which is only sparingly preserved at birth, still exists in the form of peripheral synechias. When it completely disappears it pulls the peripheral portion of the iris toward the root of the iris. Thus the iris, being increasingly stretched between the peripheral adhesions and the forming ectodermal sphincter, will suffer progressing atrophy, followed by formation of holes.

K L STOLL

Therapeutics

VITAMIN THERAPY IN OPHTHALMOLOGY A M YUDKIN, *Am J Ophth* 25:284 (March) 1942

Yudkin concludes as follows

"Throughout the discussion, no mention was made of any specific form of vitamin and I avoided speaking about the recent miraculous cures of ocular disturbances by factors of the vitamin-B group. These results have not been repeated by enough clinicians to warrant their general use in ophthalmic practice. The vitamin-B group may be obtained in concentrated form if the patient objects to brewer's yeast powder. The fish-oil concentrates may be substituted for cod- or halibut-liver oils. There is, however, no substitute for a well-balanced diet."

W S REESE

Society Transactions

EDITED BY DR W L BENEDICT

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

DANIEL B KIRBY, M D, *Chairman*

R TOWNLEY PATON, M D, *Secretary*

Jan 18, 1943

Military Ophthalmology DR W THORNWALL DAVIS (by invitation)

Injuries to the eye in war are of the same type as those in civilian life but are likely to be more severe. The conditions under which such wounds and injuries are received and treated render them more dangerous. The extremely rapid movements of troops and weapons, the much greater firing power and the aerial bombing, with tremendous explosive force, all make difficult or impossible the adequate care of wounds of all sorts, those of the eye included. Hence, although injuries to the eye in wartime are akin to those in peacetime, the facilities for their care are entirely different. It is from this point of view that observations should be made. For persons who have not had military service this is difficult.

Thermal burns constitute the great majority of all injuries to the eyes in the present war, far exceeding those in any previous one. So far, many more foreign bodies are found in the globe in this war than in World War I. Most of them are nonmagnetic.

The methods of treatment in the field of all the unspeakably horrible injuries to the eyes were discussed. Treatment at the front is medical first aid, and on its proper administration will depend the saving or loss of many eyes. Surgical treatment in hospitals for such eyes is not discussed, since this is not a military problem and differs in no way from the treatment in civilian life.

The importance of a proper understanding of color vision, night vision, anoxia and high altitude flying is discussed. Most of this knowledge is relatively new, and some of it is not yet available to members of the medical profession.

The great importance of aviation medicine, particularly the part related to ophthalmology, was emphasized.

Penicillin and Sulfadiazine in Treatment of Experimental Intraocular Infection with Pneumococcus DR LUDWIG VON SALLMANN

This paper was published in full in the October 1943 issue of the ARCHIVES page 426

DISCUSSION

DR DANIEL B KIRBY: I am interested to know how penicillin came to be employed. Can Dr Meyer say something about the chemistry of this product and the nature of its action?

DR KARL MEYER (by invitation): Perhaps I should say a few words, not so much about the chemical composition of penicillin, which is complicated and to a large extent still unknown, as about some bactericidal or bacteriostatic products of bacterial origin which have been under investigation in the last few years. Such substances have been obtained from bacteria and from molds and fungi.

The most widely known and the most thoroughly studied so far is gramicidin which was discovered and investigated chiefly by Dubos and his collaborators at

the Rockefeller Institute for Medical Research Gramicidin is a polypeptide of large molecular weight, derived from *Bacillus brevis*. It has been used locally only, since it is hemolytic and highly toxic when given systemically. It has been used in surface wounds, such as *ulcus cruris*, with excellent results. However, as my associates and I at the Institute have convinced ourselves, it is inhibited by naturally occurring substances and therefore has a limited application. Dr. Thygeson used it in a few cases of blepharitis, with discouraging results.

Other agents of bacterial origin have not been studied clinically to any extent. Most of them offer no hope because they are highly toxic, even in minute concentration, or their potency is too low.

However, penicillin, which is a yellow pigment derived from *Penicillium notatum*, has been administered to a fairly large number of patients by intravenous, subcutaneous or intramuscular injection. This work of Dr. von Sallmann's is the first in which the drug has been introduced into a body cavity by iontophoresis. Penicillin is suited for chemotherapeutic work because it is not influenced by body constituents and, further, is relatively atoxic; 1 Gm. per kilogram of mouse is the minimal lethal dose. Less than 1 mg. of penicillin has been found effective in cure of an infection with about 1,000,000 times the fatal dose of streptococci. *In vitro* the effect is still more remarkable, in that 0.00001 mg. is enough to kill between 2,000,000 and 3,000,000 virulent hemolytic streptococci. In this country, effective cures have been reported in cases of pneumococcic meningitis, staphylococcic meningitis, sepsis due to the streptococcus, staphylococcus and pneumococcus and osteomyelitis. In most of these cases previous treatment with a sulfonamide compound was unsuccessful, either because the drug was not effective or because the patient did not tolerate it.

The disadvantages of treatment with penicillin are as follows: first, there is the high cost of the product. The molds from which it is produced must be grown in rather large quantities, and the procedures of extraction and purification are expensive. However, the greatest disadvantage of the treatment is the instability of the compound. Preparations of penicillin, at least in the form of the free acid, have to be sealed in high vacuum, since they are unstable in powder form under ordinary conditions. Aqueous solutions are very unstable, and, in our experience, more than half the activity is lost after twenty-four hours at room temperature. The third disadvantage is the rapid excretion of penicillin through the kidney, so that injections have to be given at intervals of three to four hours. Chemically, penicillin is a rather strong acid, which forms water-soluble salts. This property explains, in part at least, the low toxicity and the rapid excretion. However, now there is good reason to think that the latter problem is solved, as new derivatives of penicillin have been prepared which are not water soluble and which are slowly hydrolyzed by the body enzymes.

Perhaps I should say a few words about the availability of penicillin, or, rather, its nonavailability at present. Certainly, less than 200 patients have been treated in the United States in a period of one and a half to two years. The commercial manufacture of penicillin is under government control, and only a limited amount of the substance is available, and then to a few selected clinics. It is imperative that the structure of penicillin be determined and that it be synthesized in the laboratory, and I believe this can be done. There is no question that penicillin is one of the most promising chemotherapeutic agents.

DR. DANIEL B. KIRBY: Certainly, one should not permit an agent like penicillin to be dropped without making every effort to establish its use. I believe Dr. Knapp had the opportunity to watch this experiment as it was carried out; perhaps he would like to comment.

DR. ARNOLD KNAPP: I am sorry that I cannot discuss Dr. von Sallmann's admirable presentation from the scientific point of view. I remember, however, that he told me that injuries to the cornea had occurred in some of his experiments, as this is of practical importance, I should like to ask Dr. von Sallmann to explain it.

DR LUDWIG VON SALLMANN I wish to thank Dr Meyer for the valuable information presented in his discussion. Although hope of the availability of penicillin for general clinical use in the near future seems slight, ophthalmologists are in a somewhat better position, since only about a hundredth of the average dose for a systemic infection is sufficient for the complete course of treatment of an ocular infection.

With regard to Dr Knapp's question concerning corneal damage through treatment with penicillin, it can be stated that in rabbits repeated corneal baths with a 0.25 per cent solution in five minute applications did not cause damage. Neither did the iontophoretic introduction of a 0.1 per cent solution. However, repeated iontophoretic applications of a 0.25 per cent solution produced large erosions, which usually healed in several days without residual opacity of the cornea. A 0.25 per cent solution, self instilled, did not cause any burning or discomfort. One patient treated repeatedly with corneal baths and hourly instillations of a 0.25 per cent solution did not show any harmful effect.

Topography of the Orbit with Particular Reference to Retrobulbar Injection

DR ROBERT LAMBERT and DR VIRGINIA LUBKIN (by invitation)

An anatomic study of the retrobulbar space is reported with several cross sections of normal specimens. Fluids were injected into this space post mortem, with removal and section of the entire orbital contents. Injections of 4 per cent procaine hydrochloride were made in vivo. Of several approaches to the muscle cone the preferred one is the inferior temporal. The quantity of fluid which most reliably produces analgesia of the cornea and bulb and nearly complete immobility of the globe is 3.5 cc. The first sign that the needle is in the muscle cone is dilatation of the pupil. The full effect of the injection occurs in fifteen minutes and some anesthesia lasts about an hour. The pathways taken by the injected fluid are carefully mapped. The solutions diffuse without difficulty between the muscles to the spaces outside the cone and thence forward to the lids. They also enter the episcleral space through gaps in Tenon's capsule around the entrance of the optic nerve, and may flow forward to produce chemosis. This pathway was confirmed by the observation that the globe was stained posteriorly in numerous cases of enucleation in which the procaine given by retrobulbar injection was colored with methylene blue (methylthionine chloride). A number of interesting physiologic effects, such as anesthesia of the optic nerve, paralysis of accommodation and changes in tension, are noted. The lack of necessity of anesthetization of the ciliary ganglion itself is commented on.

DISCUSSION

DR ROBERT LAMBERT In discussing this work I should like to submit a few sections and mention some practical points.

The first section is intended to demonstrate what one does not see in the ordinary sagittal section of the orbit, namely, an optic nerve nicely shown. Because of the torsion of the vessels and the nerves one rarely gets a continuous view of any structure. Therefore sagittal sections were discarded and cross sections utilized. In the second slide, at the apex of the orbit one encounters the main branches of the ophthalmic artery, which is in one of its turnings, and one sees it laterally on section. The close proximity of the four muscles is shown, with their entering nerves and structures. The thickness of the vaginal sheath is to be noted because under ordinary circumstances it protects the optic nerve from procaine or other medicaments injected.

Proceeding forward to about 1 cm. in front of the orbital apex, one can see the cells of the ciliary ganglion, which is situated between the nerve and the external rectus muscle. Still farther forward, as the muscle cone widens out, one sees the nerve posterior to the point where the central retinal artery and vein pierce the sheath. The next slide shows the point where the central

retinal vein is about to leave the nerve. The reason that anesthetization of the ciliary ganglion is not vitally important is evident since most of the structures leading to the globe are more exposed to injected substances just posterior to the globe. In another slide, taken just behind the globe, the central retinal artery and vein are present. The vein is collapsed.

One can even elevate the tension in the eye by a small injection of fluid, which is sufficient to compress the thin-walled veins and yet not sufficient to compress the heavy arteries.

The following practical points may be stressed. First, "ciliary ganglion block" should be discarded, and "muscle cone injection," as suggested by Dr. Walter Atkinson, Dr. Rudolf Aebli and others, should be substituted. We suggest that the control over tension prior to operation for glaucoma and other surgical procedures is chiefly accomplished by the use of epinephrine in the injected fluid. In the face of some contradictory evidence from other workers, I cannot positively state that the tension cannot be lowered with procaine alone, although we never succeeded in doing so. Only the injections in which epinephrine was added to the solution of procaine really lowered the tension appreciably. Control of the tension can be modified by the amount of epinephrine in the fluid injected. In my opinion, the time of injection has not been sufficiently emphasized. In pre-operative injections into the muscle cone most of the effects of the injection take place when the patient is back in his room. If one makes the injection prior to scrubbing or about fifteen or twenty minutes before operation, one obtains the full effect, including the loss of muscle power and complete paralysis of the eye. One obtains almost complete ptosis, and the eye is stationary during the operation. This, in my opinion, is a surgical advantage. Lastly, I submit that by a direct approach to the circulation in this manner more possibilities for the investigation and treatment of disease, particularly glaucoma, are afforded.

DR. ARNOLD KNAPP: Dr. Lambert said that one is apt not to wait long enough before the operation to obtain complete anesthesia from a retrobulbar injection. Such a delay, in my experience, leads to softening of the eyeball, which is not desirable, unless in the presence of glaucoma, and makes the selection of the proper interval difficult.

DR. RUDOLF AEBLI: Injection into the muscle cone was introduced by Dr. Knapp in 1884. Dr. Atkinson has reviewed the subject in his paper on local anesthesia in ophthalmology (*Tr. Am. Ophth. Soc.* 32: 399, 1934). In cases of extraction of cataract I like to make the injection just before I am ready to proceed with the section. If one waits ten or fifteen minutes after making the injection, the low tension frequently increases the difficulty of extraction.

What is the cause of the hypotony? Is it due to constriction of the vessels or to paralysis of the sensory nerve, which may in some manner influence the secretion of the aqueous from the columnar cells in the ciliary body?

DR. DANIEL B. KIRBY: I should like to have Dr. Lambert state how many experiments were done on the living subject, and what were the indications for the experiments, if there was no particular reason for ophthalmic treatment, and how many of the specimens were obtained from the cadaver.

DR. ROBERT LAMBERT: Sixty experiments were done on the cadaver in order to determine exactly where the substance was introduced, and 65 experiments were done on the living subject. The essential purpose of the experiments was to study the influence of the injections on tension, but such variations were obtained with different sites of injection and different quantities of fluid that the need first of an accurate topographic technic is apparent.

In reply to Dr. Knapp's statement, hypotony depends not only on the time of injection but on the amount of epinephrine in the injected fluid, the two most important variables I know of at present.

Bilateral Uveitis, Poliosis and Retinal Detachment with Recovery Report of a Case DR ISADORE GIVNER

This paper was published in full in the September 1943 issue of the ARCHIVES, page 331

DISCUSSION

DR LUDWIG VON SALLMANN (by invitation) Dr Givner's case of bilateral uveitis and poliosis, complicated by partial detachment of the retina and secondary glaucoma, has received an extremely thorough study. The many methods applied indicate his thoughtful approach to the diagnostic problem, and they are to me most instructive and stimulating, since they demonstrate the various possibilities that must be kept in mind in an attempt to establish the etiologic diagnosis. Although most of these tests gave negative results, they serve as a reminder that such investigations should be made under similar conditions. In suitable cases other parts of the eye may be examined, and mouse brain studies may be indicated.

The second point of interest in Dr Givner's case concerns the classification. In my opinion, it is not worth one's effort to argue on the closeness of the relation of such a borderline condition to Harada's disease or to the so-called Vogt-Koyanagi syndrome, since the etiologic factors and the specific treatment are not determined, but a disorder characterized by bilateral uveitis, scleritis and localized detachment of the retina, without meningeal symptoms, should not be diagnosed as Harada's disease as has been done repeatedly in the literature. It would be interesting to hear Dr Givner's opinion on this point of classification.

DR ANDREW RADOS Newark N J Harada's disease, described first in 1926, is an interesting and distinct entity. Clinically, the disorder has specific pathologic changes. It is always bilateral never unilateral, in contradistinction to the conditions associated with scleritis and other diseases resulting in inflammatory detachment of the retina, in which it is always unilateral. Harada's disease is closely related to the Vogt-Koyanagi syndrome, in both instances the condition is always bilateral and is accompanied by systemic changes. Furthermore, the clinical picture is characteristically so severe that recovery in the majority of cases is all the more surprising.

Furthermore, the specificity of the ophthalmoscopic picture after the uveitis has cleared is of interest. Proliferation of pigment and depigmentation is not so conspicuous in any other type of uveitis.

The etiologic factors are not known. Whether Harada's disease is a variety of the Vogt-Koyanagi syndrome has not been settled. The literature tends toward a dualistic point of view. In cases of Vogt-Koyanagi disease the uveitis itself is always more serious in the anterior segment of the eye, in cases of Harada's disease the anterior segment of the eye is usually free of symptoms, or they are slight. There are cases of Harada's disease in which no lesions of the anterior segment or only few keratotic deposits are apparent in the beginning. In cases of Harada's disease poliosis and alopecia may be present but are rare whereas in cases of Vogt-Koyanagi syndrome bilateral uveitis, poliosis and alopecia exist, and vitiligo and dysacusia may be present, but not in all instances. With the Vogt-Koyanagi syndrome, the aforementioned changes in the integument and hair not only are present but are usually bilateral, on the other hand, with Harada's disease they are usually missing, but uveitis, with the simultaneous detachment of the retina in both eyes, is present.

The histologic changes are not well known. I should like to show two slides. One is from a case of Vogt-Koyanagi disease in which enucleation was finally done, in the upper part of the slide the normal retina and the tremendous infiltration of the choroid appear. In only two other conditions is the degree of choroidal infiltration of equal severity—one is sympathetic ophthalmia and the other leukemia. In the majority of sections the infiltration consists almost solely of plasma

cells. Choroiditis with infiltration of plasma cells may indicate only the presence of an acute inflammation and is not necessarily a specific type of choroiditis, although choroiditis with the cellular elements entirely of the plasma cell type is never seen.

The high magnification in the second slide shows well the individual plasma cells forming the infiltration. If it is considered that the Vogt-Koyanagi syndrome and Harada's disease belong to the same group as sympathetic ophthalmia, as is repeatedly stated in the literature, no point of similarity except the severity of the inflammation is apparent. Sympathetic ophthalmia is one of the most severe forms of uveal inflammation. Di von Sallmann hesitated to classify Harada's disease as a separate entity because of lack of knowledge of its cause and treatment. The cause of sympathetic ophthalmia is not established either, nevertheless, it has been differentiated as a disease entity.

The cause of Harada's disease is unknown. Tuberculosis and virus infection have been suggested. There is only 1 case in which consanguinity was mentioned, that of Zentmayer. That a disease of such severity, and one in which bilateral detachment of the retina has occurred, should ever be cured spontaneously is unusual and is contrary to what happens in other types of uveitis.

Book Reviews

Reconstructive Surgery of the Eyelids By Wendell L Hughes Price, \$4
Pp 160, with 198 illustrations St Louis The C V Mosby Company, 1943

In this monograph the author presents a comprehensive review of the historical background of plastic surgery of the eyelids. The first chapter, which is devoted to the early development of skin grafting, contains much valuable information and gives the reader a clear conception of the progressive steps through which the reconstructive surgery of the eyelids has passed.

The problem of grafting without a pedicle is then considered in a similar manner with an interesting resume of the literature. Two case reports are given to illustrate the technic advocated by Wheeler of the use of a full thickness graft from one eyelid to another. The variations in types of pedicle grafts are discussed, as is the use of split skin grafts. A brief description of the sources of skin used for grafting is included in the chapter devoted to the operative technic, in which the author correctly emphasizes the importance of attention to such details as preparation of the skin to be grafted and pressure dressings.

The technic of the use of buccal mucous membrane to replace the conjunctival layer is given, as are some of the older methods of reconstruction of the tarsus. The author then reports in detail his method of reconstruction of the lower lid. In this operation the upper lid is split, and its tarsus and conjunctiva are used to line the new-formed lower lid, the skin layer of which is formed by undermining of the skin of the cheek. Several illustrative case reports with photographs demonstrate the efficiency of this technic. The freedom from additional scars, together with the normal function and excellent appearance of the newly created lid, makes this the method of choice when total reconstruction of the lower lid is necessary.

This volume is replete with illustrations, many of which are excellent, while others are poor. The case reports scattered throughout the book add little to its value. The complete bibliography, with its list of 451 references covering all phases of the subject, greatly increases the worth of the book.

It is to be recommended to all ophthalmologists, and particularly to those interested in plastic surgery.

J H DUNNINGTON

The Extra-Ocular Muscles An Outline By Wendell L Hughes, M D Second edition Paper Price \$2 Pp 32 New York Printed privately, 1939

This short pamphlet, being in outline form, is not easy reading, yet it contains an amazing amount of factual material, which probably cannot be found in any current textbook. Only one serious omission is noted. Under "Orthoptic Training," exercises for development of fusion in cases of alternating and monocular strabismus are given in considerable detail, without any mention of abnormal retinal correspondence. Apparently, the author was unaware of the disastrous results that are almost inevitable when exercises are undertaken without due consideration of the retinal correspondence. Such an omission is regrettable in a work that is otherwise sound.

Possibly the author believed that the cover test for diagnosis of a muscle anomaly has been so widely accepted that it needed only to be named. Unfortunately this is not true, and by describing other tests in detail he has failed to give the cover test its proper emphasis. To find tenotomy of a rectus muscle given as an operation of choice or even as a possibility, is an unpleasant surprise. With these few exceptions, this outline is, in my opinion, the best available survey of the better present day teachings concerning the extraocular muscles. Because

of its brevity and its disconnected form the work does not fill the great need of the beginner but it should serve as a valuable reference and as an excellent review of the subject

Persons who wish to secure the pamphlet may apply to Mrs Stewart, 218 Second Avenue, New York Eye & Ear Infirmary, New York

MAYNARD WHEELER

Vertebrate Photoreceptors By Samuel R Detwiler One of a series of Experimental Biology Monographs Cloth Price, \$4 Pp 184, with index and 110 figures New York The Macmillan Company, 1943

From time to time a book appears that contains precise technical information, presented so simply, clearly and interestingly that it makes good reading for professional and lay student alike Such is this latest publication in the series of "Experimental Biological Monographs" Although some attention is paid to the retina as a whole, it is the visual cells and retinal pigment that receive major attention

After a preliminary chapter on the vertebrate eye as a unit, the organization of the retina is described, here the reader may obtain a digest of the far reaching and revolutionary concept of Polyak concerning the types of neurons encountered in the primate retina, their synaptic relations and the paths taken by retinal impulses Succeeding chapters deal adequately with the development of retinal elements and the structure of visual cells and contain a discussion of the basis for identification of rods and cones in their more aberrant forms

From this point on, the treatment shifts from purely morphologic considerations to a discussion of functional correlations and interpretations In rapid sequence are presented the correlations between retinal structure and animal habits, the nature and degree of the positional changes through which the rods, cones and pigment of some vertebrates respond to such stimulating agents as light and temperature, and the significance of photomechanical changes, especially in regard to the duplicity theory

The later chapters doubtless hold the greatest interest and value to the ophthalmologist Two chapters are devoted to the arrangements by which visual acuity is attained, especially the significance of the fovea The correlation between foveal development and the ability to perform extensive ocular movements is accepted, but the author concludes that conjugate movements, binocular vision and partial decussation of the optic tracts are not necessarily implied He also demurs against Elliot Smith's view that the presence of a macula has led to important evolutionary advances in the portions of the brain concerned with vision Walls's recent interpretation of the fovea as a mechanism for enhancing the resolving power of the retina, not for mere optical thinness and homogeneity, is given sympathetic consideration This theory of Walls is one that cannot be ignored by any serious student who is concerned with the eye as an optical instrument

Two final chapters center about the retinal photopigments The background is painted through an exposition of the properties of rhodopsin and the less familiar porphyropsin of the rod and iodopsin of the cone The relations of these carotenoid derivatives to the A vitamins (as both precursor substances and decomposition products) are reviewed on the basis of Wald's recent, important disclosures The author identifies the Kolmer dioplets seen abundantly alongside dark-adapted rods, as retinene—the decomposition product intermediate between vitamin A and visual purple In conclusion, there is a timely digest of the dependence of vision on vitamin A, of the effect of its deficiency on physiologic thresholds (night blindness), of the breakdown of rods following prolonged avitaminosis A and of the capacity of the rods for repair after a return to an adequate diet

This monograph carries 110 excellent illustrations, several extensive tables, a recapitulation, a valuable bibliography, against which textual statements may

be checked, and both an adequate author and an adequate subject index. It contains some original data, of use as source material to the specialist. Ophthalmologists and all others interested in the retina are placed in heavy debt to Professor Detwiler for having produced a stimulating and authoritative book in a field that has been both enlarged and quickened through his own investigative activities.

L. B. AREY

Rehabilitation of the War Injured. A Symposium. Edited by William Brown Doherty, M.D., and Dagobert D. Runes, Ph.D. Price, \$10. Pp. 684. New York: New York Philosophical Library, Inc., 1943.

This volume is comprised of a series of articles by some fifty authors dealing with various phases of rehabilitation of those injured in the war. The material is divided into seven sections: viz., neurology and psychiatry, reconstructive and plastic surgery, orthopedics, physical therapy, occupational therapy and vocational guidance, legal aspects of rehabilitation, and miscellaneous subjects.

In the section devoted to plastic and reconstructive surgery the articles of greatest ophthalmologic interest include a description by Wendell L. Hughes of his ingenious method of rebuilding the lower lid and a short discussion by Dr. William B. Doherty on orbital implants. Both these papers were previously published in the *ARCHIVES* and are well known to most ophthalmologists. The Hughes operation has stood the test of time and can be recommended. The use of vitallium spheres for orbital implantation, as suggested by Doherty, is also worthy of further trial. "Practical Uses of the Tubed Pedicle Flap" is ably discussed by Sir Harold Gillies in an article replete with illustrations and concluding with a table of "conditions in which a tubed flap is preferable to a free graft." Several other papers included in this section should prove interesting and of value to ophthalmologists doing plastic surgery. The other articles dealing with ophthalmologic subjects are found in the section on occupational therapy and vocational guidance. R. C. Davenport outlines the rehabilitation of patients with nonrecoverable injuries of the eye and stresses the advisability of early treatment and individual care. Lady Duke-Elder considers the rehabilitation of patients with recoverable injuries of the eye, placing proper emphasis on the need for rapid restoration of physical fitness and the use of exercises well within the limits of the visual capacity of the patient.

This book, with its many authors, necessarily lacks continuity of style, nevertheless it contains many helpful suggestions to those interested in rehabilitation of the war injured. Some of the articles and illustrations are poor, others are very good. It is this lack of uniformity that detracts from an otherwise excellent symposium.

JOHN H. DUNNINGTON

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VISUAL FUNCTIONS IN STREPHOSYMBOLIA

SAMUEL T. ORTON, M D

NEW YORK

Children who make little or no progress in learning to read during their first two or three years in school quite naturally are often referred to the ophthalmologist, and some of them undoubtedly need corrective lenses. However, many, if not the majority, of them have adequate vision and in reality present neurologic problems. One owes a considerable debt to two English ophthalmologists—Morgan, who described the first case of congenital word blindness in 1896, and Hinschelwood, who published a small monograph on this subject in 1917. In his report Hinschelwood included several cases of acquired word blindness, as well as a group of the congenital type, and emphasized the striking parallelism between them; because of this likeness, he ascribed the occurrence of the syndrome in children to a failure of development of the cerebral cortex in the neighborhood of the angular gyrus.

In 1926 I studied several cases of delay in learning to read and was struck by the inability of the children to differentiate "b" and "d" and "p" and "q" and their tendency to read many words from right to left, instead of in the usual direction, which led to uncertainty in their distinguishing such words as "was" and "saw" and "on" and "no." I found, also, that some of them showed an unexpected facility in reading mirrored print and that some also had a native skill in producing mirror writing. To account for these observations and to bring the whole syndrome into better consonance with advancing neurologic views concerning cerebral localization, I offered the theory that the condition in these cases was not the result of a pathologic factor, such as Hinschelwood's cortical agenesis, but a physiologic deviation due to failure of acquisition of the normal adult pattern of complete dominance of one hemisphere of the brain.

In cases of loss of acquired visual functions, three distinct steps, or levels, of elaboration in the brain can be recognized. The first permits only the seeing of objects of the environment but does not tell the meaning of the things seen; the second adds the meaning of objects, maps, pictures, etc., but it requires a third step—or relay—to permit the reading of words. These three steps are recognized by neurologists in the three clinical syndromes of cortical blindness, mind blindness and word blindness. It is generally believed that it is only at the third level that the principle of unilateral dominance applies, and there are reasons for believing that at this level the records, or engrams, in the two hemispheres of the brain are opposite in sign, or antitropic, to each other and that one engram must be elided to prevent confusion. This elision of the engram of the nondominant hemisphere seems to occur only at the third, or mnemonic level, since only here does a unilateral

Read at a meeting of the New York Academy of Medicine, Section of Ophthalmology, on Feb 15, 1943

The Rockefeller Foundation is furnishing aid for the research program on which this work is in part based

lesion completely destroy function, as can be seen in cases of acquired alexia. Learning to read, therefore, according to this envisagement, entails the elision of one of the two antitropic records, or engrams, and faulty or incomplete elision would result in uncertainty in mnemonic recall of orientation and progression, such as is seen in children with congenital word blindness.

It should be remembered that these reversals of form and direction are to be seen best during the first few years of learning to read, and that after continued exposure they largely disappear, although frequently in an older child the tendency to reverse can be demonstrated by using unfamiliar letter combinations, such as nonsense syllables. The confused memory patterns which interfere with recogni-

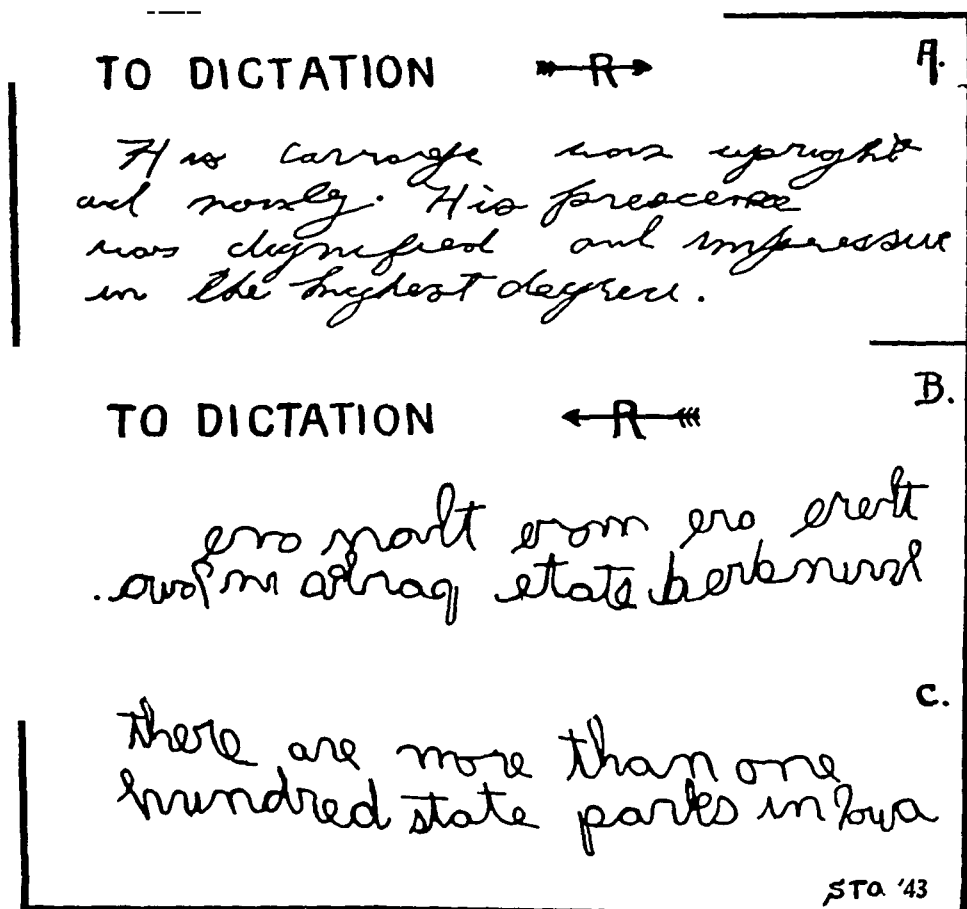


Fig 1—A, tracing of the handwriting of an 11 year old girl, written to dictation with her right hand, B, a tracing of her mirror writing, also made with her right hand, after only two or three trials of this procedure, and C, a tracing of B reversed by printing through the back of a negative, so that the product can be more readily compared with A.

tion in reading are also to be seen in the same children when they attempt to spell, and reversals in spelling persist after the child has learned to read. The most striking evidence of antitropism comes from some persons with special writing disability, in whom skill in mirror writing lies dormant and unsuspected. One of my patients who could not learn to write legibly in the common, or dextrad, direction could produce creditable mirrored script with the first attempt at sinistrad progression.

This physiologic theory offers a much more favorable prognosis than did its predecessor, and the work of my associates and myself in retraining, as well as

extended observations during the last eighteen years, has, I believe, substantiated it. As descriptive of this syndrome in cases of reading and spelling disability I offered the term "strephosymbolia," or "twisted symbols," as being less misleading, especially to the layman, than the older term "congenital word blindness." To the neurologist the term "word blindness" means a loss or lack of the ability to recognize words although vision may be intact, but to the layman the term infers an inability to see. Moreover, I believe this disorder is hereditary rather than congenital, and I much prefer to call it developmental than either congenital or hereditary.

One of the visual functions which is often discussed in connection with reading is that of eyedness. There is a common misconception that the eye selected for sighting—the master eye—is the eye with the better vision. This is not always true. As an example, 1 of my patients wore a +2.00 D. sphere and a +1.00 D. cylinder for his right eye, while for his left eye a +1.25 D. sphere and a +0.50 D. cylinder was prescribed. In spite of the greater errors in his right eye, he used this eye consistently for sighting. The master eye is usually on the same side as the master hand, but cross preferences in either direction are to be found. Sighting is a function of the extrinsic ocular muscles, which act to bring the object observed, the pupil and the fovea centralis into line. These muscles are of the striated, or voluntary, type and are under the control of the motor centers of the brain adjacent to those which control handedness. It is possible that the right or left homonymous parts of the peripheral portion of the retina might have a superior equipment and so determine the eye most apt to be attracted to a distant object and thus fix the eyedness in early infancy before binocular fusion has begun. However, the frequency with which left eyedness and ambicularity occurs in families in which there is also a preference for the left hand in some members leads me to the belief that eyedness is dependent on hereditary factors which govern the choice. It must be noted, however, that the many crossed patterns of eyedness and handedness would imply separate hereditary factors for the areas of the brain which control the eyes and those which control the arm.

The handedness pattern is open to much greater environmental influence than is eyedness, although there is evidence that the native eyedness pattern can be shifted also. Shooting a rifle was the factor in 1 such case, and my colleagues and I have observed children in whom a spontaneous shift from the left to the right eye has been noted in repeated examinations over a period of years. Some left-eyed persons can aim a rifle with the right eye only if the left eye is closed, or covered, while right-eyed persons usually learn to disregard the image in the left, or non-dominant, eye and can aim a rifle with both eyes open. In the case of a shotgun the situation is different, since without sights on the gun it may be aimed with the left eye. A priori, one might think that in aiming at a distance this would be a negligible factor, but that it does influence the accuracy of aim is recognized by gunsmiths, who build special stocks with a slight offset for those who shoot from the right shoulder but aim with the left eye. Accuracy in the use of a shotgun is said to be much improved by this procedure, and the same principle may apply in certain types of machine guns.

Some of the simpler tests of eyedness are not entirely trustworthy when used alone, and as a consequence my associates and I make use of a battery of tests to determine eyedness. In this connection it is interesting to note that the manoptoscope devised by Parsons, in our experience, frequently gives results out of harmony with those of other tests. Parsons used this instrument in his examinations on which he based his conclusion that left eyedness is evidence that a given child was originally intended to be left handed and, further, that eyedness determines which side of

the brain shall be the dominant one. He held that when left eyedness is found in a right-handed person it is evidence that training has influenced the handedness pattern and that the right-handed pattern is implanted in many naturally left-sided children because the right hand is used habitually by so large a proportion of both mothers and teachers. However, we have seen a number of left-handed children who are right eyed, whereas training right-handed children to use the left hand, either purposively or accidentally, is rare. Many persons, moreover, are neither definitively right eyed nor left eyed, and may be termed "ambocular."

In 102 patients with reading disabilities whose records I have recently reviewed, the following distribution of eyedness patterns was found: right eyedness, 40 patients; left eyedness, 37 patients; and ambicularity, 25 patients.

The left-eyed and the ambicular persons together numbered 62, as against 40 who were right eyed—obviously a much higher proportion than one would expect in the population at large. Of the 40 patients who were right eyed, 12 were either left handed or had mixed right-handed and left-handed habits. Of the 37 who were left eyed, only 5 were left handed, but 17 showed a mixture of handedness patterns or gave a history of having been shifted to right handedness in childhood. Of the whole group of 102, 69 showed a crossed or mixed pattern of handedness and eyedness, and 83 gave a family history of left handedness or of language disorders.

My interpretation of these results is that left eyedness is not the cause of the reading disability but rather indicates that there is present in these persons a tendency toward use of the right hemisphere of the brain, i. e., left sidedness. This tendency may or may not involve those parts of the brain which are of primary importance in reading. The symptoms seen in the left-eyed and in the ambicular patients do not differ from those seen in the right-eyed persons, and while covering the eye might lead to a change in eyedness, one would not expect any influence on the higher centers of the brain which are involved in strephosymbolia. Each macula is connected with both calcarine areas, and Sherrington's flicker experiments demonstrated that functionally the two eyes are interchangeable, it would seem therefore to make no difference which eye is used for sighting, since the image from either eye is probably relayed to the higher centers on both sides.

A second group of visual functions which is to be considered in connection with the reading disability includes the various refractive errors. There is no question that serious refractive disorders will interfere with reading, but many persons with minor degrees of myopia, hyperopia and astigmatism learn to read easily. Moreover, many persons with reading disability have normal refraction. When more serious errors are present, not only does their correction with appropriate lenses fail to enable the child with strephosymbolia to read without special instruction but even while he is wearing such lenses such a child exhibits the same errors of orientation and progression as do other children with strephosymbolia. This is, I believe, what one would expect on theoretic grounds. I have already mentioned the tendency to reversals in the mnemonic recall of previous exposures to the word, which must be used in order that it be recognized when it is presented again. This point is often difficult for the layman to grasp, since recognition of a word at sight seems to be simultaneous with seeing it. This, of course, is because the transmission of nerve impulses from the arrival platform to the region of the angular gyrus is too rapid to be registered in consciousness. The existence of a special zone of the cortex of primary importance in the function of word recognition is, however, clearly demonstrated in cases of acquired alexia, in which selective loss of the ability to read occurs without loss of the ability to see or of the capacity to

recognize objects, diagrams, maps, etc. These last functions are sometimes disturbed in cases of large occipital lesions which have involved the rest of the occipital cortex of both hemispheres, and acquired alexia is rarely, if ever, pure. A homonymous hemianopsia is frequent, but acquired hemianopsia can occur without alexia, and alexia is combined with it only when it involves the master hemisphere and when the lesion extends far enough forward to cut both the homolateral path from the calcarine cortex to the region of the angular gyrus and the heterolateral path from the opposite calcarine cortex by way of the corpus callosum (subcortical word blindness of Dejerine). This, again, demonstrates the adequacy of one hemisphere, since a lesion which cuts only the homolateral pathway does not cause alexia even though it is in the master hemisphere. While hemianopsia is the most common complicating picture, other symptoms, such as agraphia and varying degrees of aphasia, are also often found, indeed, in the acquired case pure alexia is so rare that some neurologists have questioned its occurrence. Persons with strephosymbolia, on the other hand, often show the alexia syndrome in exquisite purity. Handwriting may or may not be affected, and when it is not,

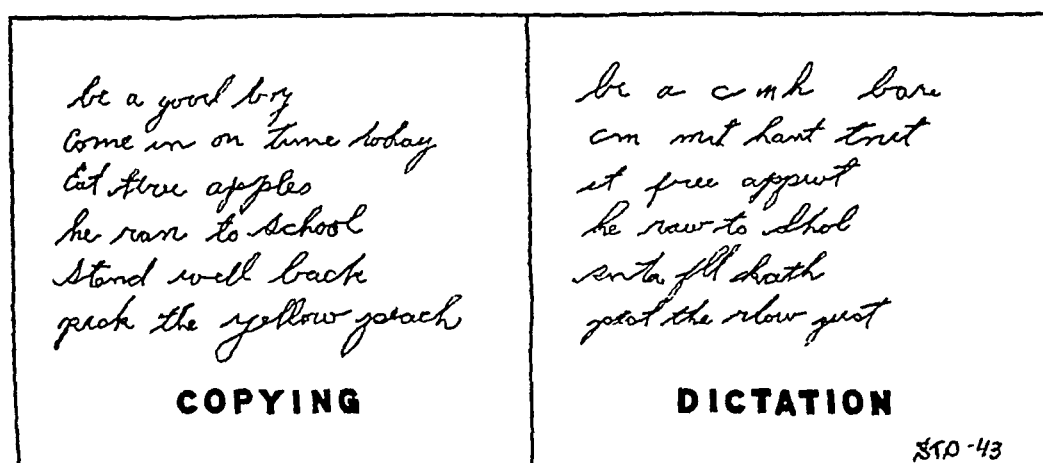


Fig 2—Carbon paper tracing of the writing of a 21 year old patient with strephosymbolia, showing the contrast between copying and writing to dictation (see "Addendum")

an illuminative demonstration of the mnemonic character of the disturbance and the adequacy of vision can be made by comparing the child's ability to copy accurately with the errors he makes in attempts to read or to write to dictation. In both these processes he calls on his visual memory, and in both he makes the typical errors of reversal. It is difficult to see how reading "was" for "saw," "ratshin" for "tarnish" or "astrep" for "repat," or how writing "ti" for "it" or "stpo" for "stop" could result from any reflective error.

The foregoing comments may, I think, be applied equally well to the heterophorias.

In a case in my experience, the diagnosis of hyperphoria was made at about the same time that I first saw the boy, when he was 11 years of age, but his family did not follow the ophthalmologist's advice and neither glasses nor treatment was provided. The boy had been in school most of the five preceding years, and while he did not have a very good basic equipment, he nevertheless had a mental age of 9 years when he was first seen and should have been able to read at the third or fourth grade level. He manifested, however, definite strephosymbolia, and his reading and spelling abilities were below the first grade norms. An intensive course of phonic retraining was instituted, after two and a half years of this treatment he had gained about a fifth grade skill in silent reading, and his oral reading and spelling were at about the fourth grade level. At this time he was seen by Dr. Conrad Berens, who found exophoria of 8 prism diopters and right hyperphoria of 1 prism diopter at 25 cm. The gain

in reading previously recorded had, however, taken place before treatment for his heterophoria was begun

In another case, that of a boy seen recently in Philadelphia, a diagnosis of exophoria was made, and sight reading methods were recommended, with definite prohibition of the phonic training which has been found so serviceable in retraining persons with strephosymbolia. This boy's father and paternal grandfather were left handed, and his mother had been a poor student, although we were unable to determine whether or not this had been due to a reading disability. The boy himself definitely favored his right hand in almost all activities but was left footed and left eyed. He was 12 years old and had been in school the usual period of years. Psychometric examinations by a battery of tests gave mental age ratings varying all the way from 9 years 7 months to 13 years 2 months. Even at the lowest of these ratings, he should have been able to read at third or fourth grade levels, but his reading achievement was that of a very low first grade level. He copied a second grade paragraph without errors, but he misread "left" as "felt," "was" as "saw," "on" as "no," "nip" as "pen" and "ton" as "not." In attempting to spell to dictation a column of simple words, he wrote "ol" for "low," "sa" for "ask," "egt" for "get," "bolg" for "belong" and "awy" for "way." When he was asked to read a simple paragraph printed in mirrored type, he accomplished this almost as rapidly as he read the ordinary print, whereas a boy of his age who had gained normal reading skills would require at least ten times as long for the mirrored passage. At the time of these examinations he was wearing the glasses prescribed for him by the ophthalmologist, who advised the sight reading teaching and interdicted the phonic training. I believe that with continuance of that proceeding the boy's directional confusion will persist and that he can be taught to maintain consistent dextrad progression only by phonic training and dextrad analysis and synthesis of words from their phonic equivalents.

I am not personally familiar with the aniseikonic disturbances, but I understand from others that patients with such disorders are by no means all nonreaders, nor do the nonreaders all show that disorder.¹

Much attention has been paid to vacillating movements of the eyes, and while bad habits in this regard might easily interfere with easy and fluent reading, it is also obvious that such a boy as the one last mentioned would scan a word from either direction in his confusion as to which way it should be read and would therefore exhibit back and forth movements of the eyes as the result of his uncertainty as to direction. Moreover, such vacillating movements would scarcely account for the confusion such children show between single letters, such as "b" and "d" and "p" and "q," or for the facility in reading mirrored print, in which constant sinistrad progress rather than alternating ocular movements is required.

Finally, the data we have assembled from the study of left handedness and of various language difficulties in the family stock of children who have a specific disability in learning to read and show the strephosymbolia syndrome give what to me is convincing evidence that such children represent intergrades between right-sided and left-sided familial tendencies and that the reading disability follows fairly definite hereditary trends. In this connection it is interesting to note that the reading disability and other language disorders are much more frequent in boys than in girls. In the current sample of 102 patients, 84 were boys and 18 girls. About the same distribution occurs for stuttering. In families with this disturbance there are also more than the expected number of left-handed members and persons with delayed speech, stuttering, reading, writing and spelling disabilities, and abnormal clumsiness (developmental apraxia). In the childhood histories of children who come to attention as presenting reading and spelling problems we not infrequently find indications of developmental deviations in their acquisition of speech and motor patterns which bear out the belief expressed herein that the strephosymbolia syndrome can best be explained on the basis of confused cerebral dominance rather than of abnormal vision.

1 Imus, H. A., Rothney, J. W. M., and Bear, R. M. *An Evaluation of Visual Factors in Reading*, Hanover, N. H., Dartmouth College Publications, 1938.

ADDENDUM—After this paper was presented at the meeting of the academy, but before it was completed for publication, I studied the case of a man aged 21 with the strephosymbolia syndrome who, in spite of having “served time” through eight grades of the public schools in New York state, had acquired less than first grade reading skill. Figure 2 shows (1) his ability to copy from print into script, demonstrating that there was no agraphia, and (2) his floundering efforts to write from dictation. This contrast demonstrates clearly that the confusion lies in the mnemonic recall and not in visual distortions. This patient is now being given remedial instruction, and his eyes are being studied by Dr. Conrad Berens. A complete report of this case, together with the results of the remedial work and of Dr. Beren’s study, will be published later.

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DISCUSSION

DR. CONRAD BERENS. I am sure that any one who has studied children with reading difficulties with or without motor anomalies and refractive errors must agree with Dr. Orton that the neuropsychologic aspects are most important and that cerebral dominance must be considered in all cases, whether or not motor anomalies and refractive errors can be demonstrated. In another paper by Dr. Orton, he said that strephosymbolia was a factor in 10 per cent of cases; it would be interesting to learn whether this is his opinion now. I have studied the history of 37 patients with reading disabilities and found 2 with a definite history of reversals. Four patients had crossed dominance. Four had convergence excess, 4 convergence insufficiency, 2 divergence insufficiency and 1 divergence excess. Hyperphoria, present in each, varied in degree. All the patients had third grade fusion. It was my impression that the motor anomalies and refractive errors of only 60 per cent were important.

There seems to be no question that the problem of conflict in cerebral dominance is important. At the same time, conflict in ocular dominance, for example a tendency to suppress the image of one eye or to suppress the images of the two eyes alternately in an attempt to maintain fusion, should also receive attention in this discussion. To my mind, it would be difficult to say in some cases whether the cerebral conflict produced by cerebral dominance is more important than the ocular conflict, which naturally has a cerebral conflict superimposed. It is not always easy to exclude certain motor anomalies, and there is no question that the ordinary tests of visual acuity and the usual tests for muscular imbalance may be insufficient without the Maddox rod test and the screen test with the eyes in the cardinal positions of gaze. In some cases the Marlow occlusion test seems to be necessary for diagnosis; it is necessary particularly in cases of corrected anisometropia in which there are associated reading difficulties. There is a certain amount of cerebral confusion when the patient attempts to fuse visual patterns of different size or quality, and it may be difficult for him to close one eye. I have found that other methods of excluding one eye in reading are often unsatisfactory.

Dr. Orton said that 1 patient selected the eye with the higher refractive error as the master eye, but he did not record the visual acuity, so that it is hard for me to determine whether this patient’s vision was poor in the right eye. I think that it is generally conceded among ophthalmologists that patients usually select the eye with the better visual acuity as the master eye, although motor anomalies, refractive errors and hand dominance must play some part.

Dr. Orton’s suggestion that hereditary factors are associated with eyedness may well be the truth in the light of what is known of hereditary ocular difficulties, especially visual and motor anomalies, and the tendency for these defects to be found in certain families.

As to Dr Orton's observation that dominance may be shifted from one eye to the other, I have seen this in several cases in which not only squint but amblyopia and the scotoma of amblyopia have been transferred from one to the other eye

There certainly is no question that ocular dominance plays a part in shooting. It is especially important in the aiming of a rifle or shotgun with both eyes open

I agree with Dr Orton that one should use several tests for the determination of eyedness. I have constructed a screen with a 1 cm perforation to be held at arm's length with both hands and found it fairly accurate. The finger point test with the right and the left index finger is useful. MacDonald's idea of placing a bent rod at the end of a head band so that the arm and hand will not be brought into the picture when the sighting eye is being determined is worthy of further study. This test is possibly more accurate for determining the master eye. I studied the master eye in relation to the landing of airplanes in the last war, and my finding was similar to Dr Orton's, that—if the tests used were valid—a certain number of persons are ambicocular

Dr Orton's interpretation of eyedness seems logical when he says "Left-eyedness is not the cause of the reading disability but rather is to be looked on as indicating that there is a tendency toward use of the right hemisphere of the brain. This tendency may or may not involve those parts of the brain which are of primary importance in reading." According to his illuminating interpretation, covering one eye and forcing use of the other would not interfere with the higher brain centers in "strephosymbolia"

Dr Orton's observation concerning refractive errors is of great interest. I am sure that many ophthalmologists have seen patients with high refractive errors who were able to read rapidly. One also sees patients who have no appreciable errors of refraction or motor anomalies demonstrable by the tests usually employed who are handicapped in their ability to read. Many of the poor readers I have seen who have had fusion disabilities and were referred for examination for this reason either had only minor errors of refraction or a low degree of heterophoria. In my experience, anomalies of accommodation, especially anisocommodation and rapid fatigue of accommodation, have interfered more with the function of reading than low degrees of heterophoria and ametropia. The patient (13 years of age) with hyperphoria referred to me by Dr Orton whose reading ability was improved by his phonetic training had 1.75 prism diopters of right hyperphoria with the Maddox rod and 3.5 prism diopters of right hyperphoria and 4.5 prism diopters of exophoria after the Marlow occlusion test. The hyperphoria was less with the eyes in the reading position, and only 1.5 prism diopters of right hyperphoria at 25 cm was measured after the Marlow occlusion test. The accommodation was remote for the patient's age, 150 to 300 mm, and it fatigued in ten minutes with the right eye and in six minutes with the left eye with several rests. The near point of convergence was 90 mm at the first examination. After two months of fusion training this was 45 mm and the prism convergence had improved from 12 to 20 prism diopters.

What bearing the heterophoria and dysaccommodation may have had on the reading disability is difficult to evaluate without a knowledge of the original findings and without a reading test of each eye separately and of the two eyes together. One should also know what the ocular movements showed while the patient was reading and whether the hyperphoria became more evident when he became fatigued, as it has been shown to do in certain patients subjected to anoxemia tests. The bearing of the allergic condition and the general physical condition is hard to evaluate from the data presented.

Dr Orton's concept of difficulties of orientation as caused by strephosymbolia seems to be logical and is the best explanation for reversal in mnemonic recall of previous exposures to a word that I know of, and his reference to the special zone of the cortex affected in acquired alexia has certainly been amply demonstrated pathologically. The fact that this difficulty is confined to reading, without

affecting the recognition of objects, is apparently more than suggestive. However, I know of no pathologic studies in congenital alexia, and I should like to know whether Dr. Orton is aware of any.

He certainly clarified the findings in hemianopsia for me, and the fact that the picture is usually complicated if the strephosymbolic patient shows pure alexia is most illuminating.

That writing may or may not be affected is a point in favor of his theory. I agree that the reversal of words in reading and writing is not a function of visual acuity and motor anomalies alone and must call on some other theory for explanation, Dr. Orton's is the most satisfying I know of.

My observation in cases similar to that of the Philadelphia boy agrees with Dr. Orton's, because psychologic tests usually show a high intelligence quotient and some of the worst readers have a mental age well above their chronologic age.

Dr. Orton brings up the question of vacillating movements of the eyes and points out that some of these unusual associated movements may be caused by the child's not knowing which way to read a word rather than by any motor incoordination. I believe this may be true in a limited number of cases, but to diagnose the presence of these unusual movements and determine their cause is often a baffling problem which requires the most careful studies. Tests under low oxygen tension with photography of the ocular movements may be required for a diagnosis of some of these movements (McFarland, R. A., Knehr, C. A., and Berens, C. The Effects of Anoxemia on Ocular Movements While Reading, *Am J Ophth.* 20: 1204-1221, 1937).

Dr. Orton has provided much food for thought, and, as is usual when any subject is discussed from the standpoint of another specialty, much has been learned. However, no acquisition of knowledge should be too one-sided, and I hope that Dr. Orton's listeners will study their patients from the standpoint of strephosymbolia but also have a complete diagnosis of their ocular, medical, neurologic and psychologic problems, with special emphasis on motivation, not overlooking hereditary factors.

DR. GEORGE H. HYSLOP (by invitation). I did not have the advantage of reading Dr. Orton's manuscript, and I missed the first portion of his talk. I heard enough, however, I think, to make two or three remarks which are perhaps supplementary to what Dr. Berens has said. The points I should like to stress are these:

In attempting to judge a patient's performance in the use of either motor or sensory functions as the application of his intelligence to them, one must consider not only the primary pathway apparatus but the higher cerebral integration. Secondly, I think Dr. Orton is the originator of the concept (though he may not entirely agree with me) that certain types of impaired language function involve not a lesion or a structural defect but an inherited functional defect. This inherited functional defect may be imitated by an acquired lesion which does affect the inborn ability of the two hemispheres to coordinate properly.

The third point is that there is no necessary correlation between the results of ophthalmologic examination and the way the patient uses his eyes, not only in reading but in judging any objects which are in the field of vision.

The last point (I do not know whether Dr. Orton would have given more attention to it if he had had more time) is that in examining children who are presumed to have defective vision because they do not read, one may note disorders of integration through studying how they use their eyes and understand the meaning of objects which are similar in size but do not involve the language function. Thus one may get a clue that there is a disorder of integration rather than of vision. A disorder of refraction or primary perception will not manifest itself as a failure of conception of a limited or specific type of object.

DR. BERNARD FREAD. It has been a privilege to hear so distinguished an authority on reading difficulties as Dr. Orton, whose name is well known not only

to ophthalmologists but to educators and other persons interested in this field I was particularly interested to hear him mention that eyedness is not so much an inheritance difficulty as the educators have indicated, and I should like to ask him whether he feels that mixed dominance, that is dominance of the left eye and right-handedness, is a factor in reading difficulties

The main thing Dr Orton stressed, which seems important, especially to ophthalmologists, is that one must have the proper physical equipment to read, that is, one must have one's optical error and muscle imbalance corrected adequately to have the proper anatomic and physiologic basis for good reading Dr Orton mentioned the nature of hemianopsia and its effect on reading There may be reading difficulties because of generally contracted visual fields Also, one has to remember there is rarely one cause for difficulty in reading and that a great deal of investigation is needed, of which some is done by the ophthalmologist and a great deal by the properly trained psychologist and educator In other words, the causes of any one patient's difficulty in reading must be multiple One must not forget the fact that poor hearing and muscular coordination influence reading, which may also be difficult for children with defects of speech The factors of illness, malnutrition, paralysis and disorders of the endocrine glands may influence reading by retarding the child's physical and mental development I must not forget the value of general intelligence and mental development, because those factors also influence reading An interesting point sometimes forgotten is that mirror reading and mirror writing, some educators feel, comprise an actual physiologic stage in the learning process of reading and need attention only when they persist

In conclusion, I am grateful to the essayist and to Dr Berens for emphasizing the fact that ophthalmologists should make careful studies of the accommodation mechanism and then refer their results to an educator interested in reading difficulties

DR LAURETTA BENDER (by invitation) May I ask what is the status of brain wave studies in regard to cortical dominance?

DR SAMUEL T ORTON I do not think I have much to offer in closing the discussion Dr Berens spoke of finding reversals in a small number of the non-readers he studied I would assume that he saw older children or adults, and I would expect that As one attempts to teach a child, the child gradually gets the direction straightened out, but still there is enough confusion in direction so that the recall of a word is not accurate One finds that the more accurate recall frequently lags behind the amount of recall necessary for recognition of a word, so that the child learns to read before he learns to spell Persons with reading difficulties are usually poor spellers

Dr Berens spoke of the case to which I referred in my paper I have no record of the visual acuity I gave all the details I had

He also spoke of testing for eyedness with a screen with a hole in it I have been using a comparable test for quite a while A card about 6 by 8 inches (15 by 20 cm) with a hole in the center somewhat smaller than a dime is used It is offered first to the child with the examiner holding it with the hole over the bridge of the nose, so that the child must shift the head to bring one eye into line Then the child is asked to hold it, first with one hand, then with the other and then with both Occasionally one finds that the hand used influences the choice of the sighting eye, but commonly if the child has a dominant eye he will shift the card over in front of that eye One finds some unusual responses, but I feel that with first the examiner and then the child holding the card one generally gets valuable data to be added to the results of the other tests used for eyedness

Dr Berens asked about the pathologic observations There are none yet I have done a great deal of work in brain pathology and have examined 1,500 or more human brains, and among these I have not yet seen a selective agenesis of the

type that Hinschelwood suggests. I have seen one hemorrhage in the angular gyrus in an infant's brain in which there were multiple hemorrhages.

In a survey of a whole community my associates and I found reading disabilities sufficient to retard development at least one year in 10 per cent of the total school population. If this proportion was true and reading difficulties were due to agenesis one certainly would find such a defect in the angular gyrus frequently in a series of 1,500 brains. Such a fault in development in the region of the angular gyrus would have to be present as a bilateral lesion in children to cause the reading disability, and I have not observed a brain with this selective agenesis in even one hemisphere.

Dr Hyslop spoke of the matter of integration, and that is a point of great importance. I mentioned the fact that it is only when integration takes place at the third, or word, level that reversed memory pictures come out, and it is in the integration process that these reversals occur.

Dr Fread asked a question concerning mixed dominance. I thought I had expressed the opinion that the mixture of dominance is not a causal factor but does give evidence that the child is not all right sided or left sided as far as the brain is concerned, and I am coming to the conclusion that there are a lot of persons who are not entirely one sided, who do not have all the motor functions organized in one hemisphere, in whom the dominance for some functions is in one hemisphere and that for some in the opposite. I am supported in this belief by observations made by Dr Nielsen, a neurologist of Los Angeles.

Dr Fread also brought up the question of intelligence. Of the 102 persons on whom I reported, none had an intelligence quotient below 90. All patients with an intelligence quotient below 90 were ruled out so that confusion due to the problem of intelligence would be excluded.

I agree with Dr Fread as to the fact that reversals are present in almost all children when they are first learning to read. Almost all children are confused at first between "b" and "d," etc., but the confusion does not persist as it does in children with strephosymbolia.

In answer to Dr Bender's question, I may say that I have not had an opportunity to work in the field of electroencephalography as yet but hope to soon.

TRAUMATIC ENOPHTHALMOS

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Although fracture has always been regarded as a cause of enophthalmos, there exists in the literature considerable speculation on the mechanism of the displacement of the eye when there is no external evidence of fracture. Most of the discussion on the sometimes distressing consequences of a blow on the eyeball took place before the roentgen rays were developed to a high point of usefulness. To many of the early observers fracture meant fragmentation and gross deformity. It was inconceivable to them that the eyeball could receive, withstand and transmit a blow forceful enough to fracture any of the walls of the orbit. Since means of demonstrating deep, or internal, fractures were lacking and, in later years, since roentgenography was not employed at its greatest efficiency, enophthalmos in many cases was considered an extraordinary phenomenon. Today, with the roentgen rays, one is able to study the orbit in fairly minute detail, and considerable knowledge of the changes which occur in this cavity in disease and in injury has been gained. With roentgenography the cause of enophthalmos has been clarified, and another indication of the value of the roentgen rays in ophthalmic practice has been added to a growing list.

In a recent reference to traumatic enophthalmos, Benedict¹ listed the following causes as responsible for varying degrees of enophthalmos:

- 1 Dislocation of the trochlea²
- 2 Atrophy of orbital fat (trophoneurotic theory of Praun³ and Beer,⁴ mentioned by La Grange,⁵ Gessner,⁶ Lukens⁷ and others)
- 3 Enlargement of the orbit (Lang⁸ and others)
- 4 Cicatricial contraction of retrobulbar tissue (Praun,³ La Grange,⁵ Lederer,⁹ Le Roux¹⁰ and Luniewski¹¹)
- 5 Rupture of orbital ligaments or fascial bands (Kilburn,¹² Fick,¹³ Collins,¹⁴ Shoemaker,¹⁵ Morax¹⁶ and Rand and Reeves¹⁷)

Read before the American Ophthalmological Society, Hot Springs, Va., June 11, 1943.

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1 Benedict, W. L., in Berens, C. *The Eye and Its Diseases*, Philadelphia, W. B. Saunders Company, 1936, p. 330.

2 Hughes, W. L. Personal communication to the author. In the operation of recession of the trochlear nerve introduced by Hughes, enophthalmos was not of measurable degree in any of the cases.

3 Praun, E. *Die Verletzungen des Auges*, Wiesbaden, J. F. Bergmann, 1899.

4 Beer, T. *Arch f Augenh* **25** 315, 1892.

5 La Grange, F. *Les fractures de l'orbite*, Paris, Masson & Cie, 1917.

6 Gessner, C. *Arch f Augenh* **28** 297, 1888.

7 Lukens, C. *Ophthalmology* **3** 30, 1906.

8 Lang, W. *Tr Ophth Soc U Kingdom* **9** 41, 1889.

9 Lederer, R. *Arch f Augenh* **53** 241, 1902.

10 Le Roux, H., and Maklakoff. *Arch d'opht* **24** 176, 1904.

11 Luniewski, S. B. *Post okul* **5** 47, 1903.

12 Kilburn, H. W. *Arch Ophth* **31** 384, 1902.

6 Fracture of orbital wall (Lederer,⁹ Lang,⁸ Praun³ and others)

7 Displacement of part of orbital tissue (Lang⁸ and others)

As enlargement of the orbit and displacement of part of the orbital tissue could occur only as a result of fracture, three of the aforementioned points pertain to deformity of the bony orbit resulting from violence. Lang's contention that fracture occurred in every case of enophthalmos and that the displacement was probably due to all three of these conditions corresponds precisely with my experience. Lang, in discussing his 2 cases in 1889, stated

I would suggest that the injury may have produced a fracture and depression of a portion of the orbital wall, the orbital fat would then be no longer sufficient in quantity to fill this enlarged postocular area without a sinking in of the globe from atmospheric pressure and the resulting limitation in the ocular movements. These cases might then be considered as less exaggerated but similar to those of von Becker and Tweedy.

In von Becker's and in Tweedy's case the injury was produced by a cow horn's driving the globe into the antrum through a perforation of the floor of the orbit. In both cases the eyes were lost from view. Lang's opinion was stated without aid of surgical exploration, autopsy examination or, of course, roentgenography.

MATERIAL

Of 120 cases of fracture of the bones of the face in which the orbit was involved in some way, enophthalmos was present, or developed subsequent to the injury, in 53 (table 1). Fracture of the orbit was noted in every case of traumatic enophthalmos through a period of ten years. In 29 cases external deformity or severe fracture involving the margin of the orbit, with dislocation of fragments, occurred and the cases are not included in this study. In these cases fracture was obvious clinically and/or roentgenographically. In 24 cases the fracture was internal, or deep in the orbit, unassociated with solution of continuity or deformity of the margin of the orbit or of surface structures. This series of 24 cases (table 2), of the type which was inexplicable to the older authors, forms the basis of this report.

In all these 24 cases there was displacement of the eye of 1 to 9 mm without other external deformity, as measured by the Hertle exophthalmometer. In most of the cases the eye was displaced posteriorly 2, 3 or 4 mm. In the cases of more severe injury, of the 24, the eye was displaced posteriorly and inferiorly. In 2 instances the eye was displaced posteriorly and slightly nasally. The displacement of the eye would have been overlooked clinically in a number of cases if the exophthalmometer had not been used on the suggestion of the roentgenographic report after the signs of recent trauma had subsided.

In the cases of severe displacement enophthalmos was apparent early. In 1 case in which I made examination the day after injury, the eye could scarcely be seen when the greatly swollen lids were pried open. In 2 other cases in which the enophthalmos was not severe, the displacement was apparent on the third and fourth days, when examination was made after the roentgenographic report was rendered. But, in most of the cases, because of hemorrhage, edema and/or air in the orbit, the displacement was not found until two or three weeks had passed.

13 Fick, A. E. *Diseases of the Eye and Ophthalmoscopy*, Philadelphia, P. Blakiston's Son & Co., 1896.

14 Collins, E. T. *Brit M J* 2:846, 1899.

15 Shoemaker, W. T. *Am Ophth* 9:391, 1900.

16 Morax, M. V. *Bull et mém Soc franç d'ophth* 47:391, 1934.

17 Rand, C. W., and Reeves, D. L. *Surg, Gynec & Obst* 69:460, 1939.

The eye was exophthalmic at first in several cases. In general, it may be said that the severity of the early signs of violence to the eye bears no relation to the degree of injury delivered to the walls of the orbit.

TABLE 1—*Data on Cases of Fracture of the Orbit Studied Roentgenographically Through a Ten Year Period*

Total number of cases of fracture	120
Total number of cases of traumatic enophthalmos	53 (44%)
Cases of combined external and internal fracture	29
Cases of internal fracture	24 (45%)

TABLE 2—*Essential Data on the Twenty-Four Cases of Internal Fracture of the Orbit Causing Enophthalmos**

Case No	Patient	Injurious Agent	Degree of Enophthalmos, Mm	Walls Fractured	Depression of Floor into Antrum, Mm	Eye † Involved and Visual Acuity	Diplopia Present	Permanent Injury to Eyeball
1	F B	Fist	3	Inferior nasal	9	O S 20/20	Yes	None
2	E W	Fist	2	Inferior	6	O D 20/30	No	None
3	A W	Fist	9	Inferior	Complete	O D 20/30	Yes	None
4	L T	Fist	5	Inferior nasal	15	O S 20/20	Yes	None
5	L A	Fist	3	Inferior nasal	8	O S 20/20	No	None
6	O J	Fists	O D 4 O S 6	Inferior	14	O D 20/15	Yes	None
				Inferior	16	O S 20/15		
7	J O	Skid	5	Inferior nasal	14	O S 20/50	Yes	Hole in fovea partial optic nerve atrophy
8	J B	Automobile accident	6	Inferior	18	O S 20/20	Yes	None
9	J K	Fist	3	Inferior nasal	8	O S 20/200	No	Retinitis sclopetaria
10	C S	Gouging	1	Inferior	4	O S 20/40	No	Hemorrhage in vitreous, chorioretinal atrophy
11	G T	Knee	2.5	Inferior	7	O D 20/20	No	None
12	H M	Fist	2	Inferior nasal	7	O S 20/30	No	None
13	E H	Cow's horn	7	Inferior nasal	20	O S 20/20	Yes	None
14	S	Fist	3	Inferior	10	O D 20/20	No	None
15	W W	Automobile accident	2	Inferior nasal	7	O S 20/20	No	None
16	W R	Fist	4	Inferior nasal	10	O D 20/40	No	None
17	M O	Fist	6	Inferior	14	O D 20/30	Yes	None
18	J L	Baseball	2	Inferior nasal	5	O S 20/30	No	None
19	S C	Automobile accident	3	Inferior	8	O S 20/20	No	None
20	W W	Fist	7	Inferior	Complete	O S 20/70	Yes	Paralysis of third nerve, partial optic nerve atrophy
21	A W	Golf ball	3	Inferior	6	O D 10/200	No	Retinitis sclopetaria
22	M G	Fists	3.5	Inferior nasal	9	O S 20/20	Yes	None
23	E M	Automobile accident	2	Inferior	6	O S 20/20	Yes	None
24	T T	Fist	4	Inferior	12	O S 20/20	No	None

* In 14 instances the fracture was due to the blow of a closed fist. The floor was fractured in all cases, and the nasal wall in addition in 11 cases. On calculation it was found that 1 mm. of enophthalmos indicated an average depression of 3 mm. of the floor of the orbit into the antrum. Diplopia was experienced in 11 cases. Permanent impairment of vision of the eye of the involved orbit was suffered in only 5 cases.

CAUSES OF FRACTURE

The circumstances responsible in these cases of internal fracture of the orbit were varied. It may be a matter for some surprise that in 14 instances the fracture was produced by a blow of the fist. Many of the patients were treated first for the ordinary "black eye." In most of the cases in which roentgenographic studies were made for this complaint fractures were found, and in those which

could be followed enophthalmos of 2 to 9 mm developed. In 1 of the cases of most severe enophthalmos (case 3) the displacement resulted from the blow of a fist, and the case will be described in detail. In case 2 fracture of the floor of both orbits with bilateral enophthalmos resulted from an assault. Many of the patients with this injury were uncooperative, so that final notes were difficult to obtain, otherwise, this series would have been many times larger. Automobile accidents were responsible in 4 of the cases. In 3 cases the injury was received while the victim was playing football. In 1 case the patient was struck by a baseball, in 1 by a ski, in 1 by a golf ball, and in 1, by a cow's horn.

ROENTGENOGRAPHIC FINDINGS

The roentgenographic findings were characteristic. In every case the floor of the orbit was broken through into the maxillary sinus below. Fragments could usually be seen in this sinus, and the increased density of orbital tissue was always demonstrable, the tissue prolapsing in some degree into it. In the cases of severe enophthalmos the antrum was densely and completely clouded by the orbital tissue which filled it. The thin fragments of bone displaced into the antrum in these cases were the only trace of the floor of the orbit that could be found. In several of the cases of less severe displacement the infraorbital canal seemed to have braced the floor and stopped the descent of tissue. The degree of prolapse and the resulting enophthalmos seemed in several cases to have been determined in part by the size of the antrum. In the cases of severe displacement the antrums were large. In 15 of the cases deformity of the nasal wall of the orbit was apparent, in addition to fracture of the floor. The ethmoid cells were compressed by the medial displacement of the lamina papyracea in these cases. In all the cases the effect of the fractured walls was to increase the capacity of the orbit.

Fracture or deformity of the floor of the orbit can be recognized in the roentgenogram of the skull in the Caldwell position, especially when corresponding parts are compared. The degree of prolapse into the antrum can be observed better in the Water position. Good roentgenographic technic is essential.¹⁸ The clouded appearance of the antrum caused by the presence of orbital tissue may be mistaken for the appearance most commonly produced by sinusitis. Obviously, fragments of bone are never seen in the antrum involved by the latter condition.

MECHANISM

The mechanism of the internal orbital fracture responsible for the posterior displacement of the eye is quite clear. From the nature of the fractures it is evident that the force of the blow received by the eyeball was transmitted by it to the walls of the orbit, with fracture of the more delicate portions. That the floor is always involved is quite understandable. The posterior convex portion of the floor bulges upward back of the eyeball in a position to receive most of the force transmitted by the eye. The floor is of very thin bone, similar in weight to the lamina papyracea—a fact easily demonstrated by transillumination of the dried skull—and is braced but slightly by the infraorbital groove, or canal. In the cases of less severe enophthalmos the posterior portion is fractured, and in the cases of more severe displacement the entire floor is broken through. It is usually in the latter cases that fracture of the lamina papyracea is also observed. The effect of these fractures is to increase the capacity of the orbit, and through the fracture of the floor tissue is

¹⁸ Pfeiffer, R. L. *Tr Am Ophth Soc* 39:492, 1941.

allowed to prolapse into the antrum, with resulting enophthalmos. If the antium is large enough it is possible for the eye to drop into it and disappear from view.

In all of the 24 cases the force of the blow was concentrated in a small area so that it struck the eye directly and was not buffered by the protective projecting structures of or the structures adjacent to, the margins of the orbit.

SYMPTOMS

In half the cases, except for the acute signs of injury, distressing symptoms other than the displacement of the eye were not experienced. In 11 cases the patient did not know that the eye had been displaced, and in these cases there were no other symptoms. Limitation of motility occurred, and diplopia was bothersome in 11 cases. In 5 cases paresthesia of the face resulted from the fracture of the infraorbital canal and rupture of the infraorbital nerve. This symptom soon seemed to disappear from the patient's mind.

That the eye is able to withstand such severe trauma and retain its visual function, as was true in most of the cases, is indeed remarkable. Central vision was destroyed in only 4 cases. In 1 case there was a hole in the macula, in 1 case a hemorrhage in the vitreous, with unknown termination, and in the remaining 2 cases, rupture of the choroid and disorganization of the central area of the retina. In several instances reduction of visual acuity occurred to some degree. Dislocation of the crystalline lens was not noted, and detachment of the retina did not occur during the follow-up period. In many cases, however, the retina showed evidence of contusion when it was first examined. Commotio retinae, retinal and preretinal hemorrhages, iritis, dilatation of the pupil, subconjunctival hemorrhage, hypotony, edema and ecchymosis of the eyelids and orbital emphysema were the most common early signs. Rupture of the eyeball was not noted.

ILLUSTRATIVE CASES

For purposes of illustration, several cases are described briefly, with reproduction of the roentgenograms. The first case is fairly characteristic of most of the series, the second was one of bilateral enophthalmos, and the third was an instance of severe deformity.

CASE 1—F. B., a woman aged 30, had been struck on the left eye with a closed fist in an altercation with her husband four months before. The eye was greatly swollen and was black and blue for days. Since this episode the eye had seemed to the patient to be "in too far." There was no double vision. Numbness of the left side of the face was no longer bothersome (fig. 1).

Examination—The left eye was set deep in the socket, with a hollow space beneath the eyebrow. The pupils were equal and active on the two sides.

Vision was 20/20 — 3 in the right eye and 20/20 — 1 in the left eye.

The exophthalmometric reading was 18 mm for the right eye and 15 mm for the left eye. The palpebral fissure measured 9 mm in width in the right eye and 7 mm in width in the left eye.

There was orthophoria for near vision. No diplopia was brought out with the red glass. There was good motility in each eye.

The fundi were normal.

Roentgenographic Report (fig. 2)—Stereoscopic roentgenograms of the orbits showed that the margins were symmetric and of the mesosemic type. The sphenoid ridges, the superior orbital fissures and the temporal lines were also symmetric. The floor of the left orbit was fractured and was displaced inferiorly at least 1 cm into the antrum. The nasal wall of the left orbit was concave and displaced nasally, compressing the ethmoid cells. The capacity of the left orbit therefore, was much increased. There was no external evidence of fracture of the bones of the face. The right orbit was normal. The optic canals were circular, measured 5 mm in

diameter and were symmetric. All the paranasal sinuses were clear except the left antrum, which showed prolapsed orbital tissues.

Impression—The impression was that of fracture of the left orbit, involving the floor and the nasal wall, with prolapse of orbital structures into the left antrum, this displacement accounting for the enophthalmos.

Diagnosis—The diagnosis was enophthalmos of the left eye, resulting from internal fracture of the orbit.

Indication—The patient was not bothered sufficiently by the displacement to feel that an operation to restore the eye to a normal position was justified.



Fig 1 (case 1)—Photograph of patient, showing the enophthalmos of 3 mm of the left eye.



Fig 2 (case 1)—Roentgenogram of orbits, showing the fracture of the floor of the left orbit, with prolapse of fragments and of orbital structures 9 mm into the antrum.

CASE 2—O. J., a Negress aged 23, had been attacked three years before, when she suffered severe blows to the face and eyes. Since the attack the eyes had seemed sunken and double vision had been persistent, especially on looking upward.

There was weakness of the left superior rectus muscle, with pronounced secondary overaction of the right inferior oblique muscle.

Examination—Vision was 20/20 in the right eye and 20/30 in the left eye, with correction it was 20/15 in the right eye and 20/15 in the left eye.

The exophthalmometric reading was 14 mm for the right eye and 12 mm for the left eye.

The interpalpebral fissure measured 6 mm in width in the right eye and 5 mm in width in the left eye.

Double vision was present and increased when the eyes were turned up and to the left. The fundi were normal.

Roentgenographic Report (fig 3)—Roentgenograms of the orbit showed the margins to be symmetric, uninterrupted and of the mesoseme type. The sphenoid ridges, the superior orbital fissures and the temporal lines were also symmetric. The floors of both orbits were fractured, and fragments of bone could be identified in the antrums below, with prolapse of orbital tissue, approximately 18 mm or more, into each antrum. The lamina papyracea of the left orbit was deformed with compression of the ethmoid cells posteriorly. The optic canals were nearly circular, measured 5 mm in diameter and were symmetric and normal.



Fig 3 (case 2)—Roentgenogram showing fracture of the floors of both orbits, with prolapse of fragments and orbital structures into both antrums.



Fig 4 (case 3)—Photograph of patient, showing severe enophthalmos of the right eye, resulting from the blow of a fist.

Diagnosis—The diagnosis was bilateral traumatic enophthalmos, more severe on the left side.

Operation—Myectomy of the right inferior oblique muscle was performed.

Result—The diplopia was relieved and the patient was content with the result.

CASE 3 (fig 4)—A W, a woman aged 25, was struck on the right eye by a fist in February 1942 and was unconscious for a few minutes, with some bleeding from the nose and mouth. Numbness on the right side of the face resulted from the blow, at the time of examination it was less bothersome. The eye was swollen shut for three weeks, when the swelling subsided, the sunken condition of the right eye was first observed. This progressed until July 1942. Vision had been preserved, but double vision was most annoying.

Examination—The right eye was displaced posteriorly and inferiorly. A deep hollow space lay beneath the brow. The pupils were active and equal on the two sides.

Vision with correction was 20/30 + 2 in the right eye and 20/30 in the left eye. Exophthalmometric readings were 9 mm in the right eye and 18 mm in the left eye. The palpebral fissure measured 4 mm in width in the right eye and 9 mm in the left eye.

There was restricted activity of the external and the superior rectus muscle and of the inferior oblique muscle on the right side.

Diplopia increased in the fields of action of the external rectus, the superior rectus and the inferior muscles of the right eye.

Anesthesia was present over the right malar area.

Roentgenographic Report (fig 5)—Stereoscopic roentgenograms of the orbits showed that the margins were symmetric and without evidence of solution of continuity. There was complete destruction of the floor of the right orbit, with absence of visible fragments. The underlying antrum was densely clouded, and the soft tissue shadow suggested the prolapse of the orbital content into it. The lamina papyracea showed deformity, with compression of the ethmoid labyrinth and adjacent structures.

The impression was that of complete fracture of the floor of the right orbit and nasal wall with prolapse of orbital structures into the antrum.



Fig 5 (case 3)—Roentgenogram of orbits, showing fragments of the floor and the orbital content filling the right antrum. The orbital margin and the adjacent structures are unaffected.

TREATMENT

Most of the patients with enophthalmos did not experience concomitant symptoms, and measures for correction of the displacement of the eye were not required. Indeed, several patients were unaware that the deformity existed. Several were much more interested in securing relief of diplopia than in having the eye restored to its normal position. For these patients measures to correct the diplopia were sufficient and gratifying.

Treatment to correct the deformity is receiving attention. Many procedures may be conceived for the reconstruction of the floor of the orbit and the restoration of the eye to its proper position. The use of autogenous tissue, bone or cartilage to form a new floor or of fat to fill the antrum, and thus raise the eye and orbital tissues, seems most likely to succeed. To fashion a new floor of viable tissue certainly requires consummate skill to overcome the technical difficulties. Filling of the defect in the floor of the orbit with fat taken from the abdominal wall is a relatively simple procedure but may not prove permanent. The use of preserved fascia lata in 1 case failed, for it acted as foreign material and had to be removed.

SUMMARY

Patients exhibiting signs of recent injury, such as the ecchymosis and edema of a "black eye," should have a roentgenographic examination for possible internal fracture of the orbit. The development of enophthalmos after trauma is always an indication of fracture, usually of the floor and/or the nasal wall, frequently without solution of continuity of other parts of the orbit. The posterior displacement of the eye is due to the increase in the capacity of the orbit, which results from the fragmentation of the floor with prolapse of orbital content in some degree into the antium, and to fracture of the lamina papyracea with compression of the ethmoid cells.

Treatment may not be needed if the enophthalmos is not severe. If diplopia is present, in cases of less serious displacement the simpler means of relief may be operation on the extraocular muscles. In cases of severe enophthalmos operation to raise the orbital structures from the antium may be gratifying to the patient.

CONCLUSION

Enophthalmos following trauma is due to fracture of the orbit. Internal fracture of the orbit, usually of the floor, without involvement of the margin, is a frequent result of a blow on the eye and should be diagnosed by roentgenographic means.

635 West One Hundred and Sixty-Fifth Street

RECURRING ATTACKS OF CONCOMITANT EXOTROPIA, EACH FOLLOWED BY TRANSIENT ESOTROPIA

MIGRAINE THE PROBABLE CAUSE

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The present case is reported because it may throw light on the convergence mechanism and because, so far as I have ascertained, no such case has previously been described. However, the literature on oculomotor anomalies is so voluminous that reports of even a considerable number of such cases could easily be overlooked. No doubt cases of the kind have been observed but not reported. In fact, a colleague described to me a case which, judging from his brief account of it, was closely similar. The condition is not described in textbooks.

REPORT OF A CASE

An unmarried brunet, a Jewess, first consulted me on April 2, 1936, at the age of 28, and I have seen her at frequent intervals ever since. She complained of attacks which had begun to occur about seven months before her first visit to me. During an attack "everything looked crooked, people's faces looked queer" and her eyes "looked funny" to her friends. As will be evident, these phenomena were dependent on attacks of pronounced exotropia followed by transient esotropia. Up to the present she has had about twenty-four such attacks. Her refraction was as follows. In the right eye vision was 20/40, and with a correction of -0.50 D sph $\ominus -0.50$ D cyl, axis 105 it was 20/20—, in the left eye vision was 20/40, and with a correction of -0.75 D sph $\ominus -0.37$ D cyl, axis 90 it was 20/20—.

Between attacks, she had orthophoria within 2 prism diopters as indicated by the objective cover and the Maddox rod test. Hyperphoria never exceeded 1 prism diopter. Ocular movements were normal in all directions. She could overcome a prism of 14 D base out and could not overcome one of more than 6 D, and sometimes not one of more than 2 D, base in. The near point of convergence was at 6 cm. With my new test, her acuity of stereopsis was 20/30. Her fundi and visual fields were normal. Her pupils were equal and round, they measured 2.5 to 3 mm in diameter and reacted well to light but poorly in convergence. Her irises were dark brown.

Thus far the ocular attacks have consisted of two series separated by an interval of three and a half years. The first series covered a period of about one year, consisted of at least seven attacks and ended about Aug 1, 1936. The second series, consisting of seventeen attacks, covered a period of one and a half years, beginning July 14, 1940 and ending about Dec 1, 1941. Since then she had had no attacks, an interval of one and a half years at the time of writing. The interval between two attacks was often very short, the shortest being about one week.

I have never had the opportunity of examining her daily throughout an attack but have seen her several times during many of her attacks. I have seen her in every phase of an attack and frequently also in the intervals. According to her statements and my own observations, the attacks were all essentially alike. Three hours after she thought an attack had begun, exotropia of 40 prism diopters had developed in the left eye. The next day the exotropia was still 40 prism diopters. On the third day it was 30, and on the fourth, 20 prism diopters. Even when the exotropia was 40 prism diopters, she frequently overcame it and obtained bifixation, but only with the aid of excessive accommodation, which reduced her distance vision to 20/200. During fixation her visual acuity could be restored by the addition of a -1.50 D sphere to her usual correction. For near range she had clear vision and bifixation without this addition. Her near point of convergence was at about 15 cm. The exotropia was as constant and as closely concomitant as that in an ordinary case of concomitant strabismus, although there was slight limitation of inward motion for each eye. When the

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exotropia had become 15 prism diopters, bifixation reduced the visual acuity to 20/50 — With exotropia of 30 prism diopters and bifixation, it required fifteen seconds for vision to clear when one eye was covered. When the eye was uncovered, bifixation with blurred vision was achieved somewhat more quickly.

About one week after the onset of an attack, a stage was reached in which, during the examination, she sometimes had about 4 prism diopters of exophoria, and sometimes 4 prism diopters of esophoria. On one occasion, while she was being tested, she at first had orthophoria and then, for a few moments, as much as 8 prism diopters of esotropia. This stage I shall call the interphase of an attack. After this, relatively constant left esotropia developed, with diplopia, which disappeared in about a week. Sometimes a slight amount of esophoria persisted for a week longer. The greatest amount of esotropia I observed was 15 prism diopters. With this there was slight limitation of outward motion of each eye, and the convergence near point was at 375 cm. On one occasion diplopia was found to begin at a distance of 61 cm. There was never diplopia at the reading distance. In two attacks, with esotropia of 15 prism diopters, I found ortholaterophoria at 33 cm with the vertical diplopia test.

In eight attacks I observed transition from exotropia to esotropia and I therefore assume that it occurred in all attacks. However, the patient thought that the first attack of the second series began with diplopia, and when I saw her on the following day she had esotropia of 8 prism diopters. During the exophoric phase she never observed diplopia, even when there was persistent exotropia. She also did not notice diplopia in the esophoric phase until I elicited it in my office. After this, she always observed diplopia when there was esotropia. She learned to distinguish the two phases by the fact that in the exophoric phase vision became blurred when things did not "look crooked" and that in the esophoric phase she had diplopia and distinct vision. Near vision, she thought, was never disturbed in either phase.

Although I proved to her that she could relieve her ocular discomfort at any time by occluding one eye, I could not induce her to employ this procedure because she thought it might cause her to "lose her job." I prescribed glasses containing an addition of a —1.75 D sphere to her usual correction, to be used during the exophoric phase, but she seldom used them, although they gave her clear vision for distance.

With either eye occluded, distance vision was always the same, and the range of accommodation was 7 D. Hence in neither phase of an attack was there paresis or spasm of accommodation. The pupils during the attacks remained about the same size as before and responded well to light, and during the exophoric phase they responded as usual in convergence. During the esophoric phase their response in convergence was diminished, probably because then less effort was needed for convergence. At no time was nystagmus, mydriasis or definite miosis observed.

As a rule, hyperphoria was not revealed by the Maddox rod test during an attack. However, during several attacks she had left hyperphoria of 1 to 2 prism diopters. In one attack I found, with exophoria of 30 prism diopters, left hyperphoria of 8 prism diopters by the objective cover test. At or near the end of the esophoric phase of one attack, I once noted ortholaterophoria and 3 prism diopters of left hyperphoria with the Maddox rod test.

The patient stated that just before and during an attack she had a feeling of extreme fatigue. At or near the onset she had headache and nausea, and in some of the later attacks she vomited. The headache began over the left eye and spread to the upper jaw and then to the region of the left mastoid and left side of the occiput. She complained that there was sometimes a "terrific weight on the back of [her] neck, drawing [her] down." The headache did not prevent sleep and persisted two to four days. As a rule, its severity had greatly abated by the time the interphase was reached, and during the esophoric phase she did not complain of the pain.

She began to have headaches about ten years before I first saw her, and for the first few years they were not severe. Those associated with strabismus seemed to bear no constant relation to the menstrual periods, but the others occurred almost exclusively at these periods. She had never had scotoma of scintillating or any other type. At the beginning of a headache she frequently had a feeling of irritation as if from a foreign body in the left eye. With a severe headache she sometimes complained of peculiar feelings in one or the other arm. Shortly after the second series of ocular attacks ceased, she had a few attacks in which the "cords in the shoulder swelled," associated with a peculiar feeling in her throat and momentary difficulty in talking and swallowing. During the interval of three and a half years in which she had no ocular attacks, she had many attacks of headache with nausea, and such spells have been frequent during the present interval.

The patient is the fourth of 5 children, the others are all males. The second brother has frequent attacks of severe migraine associated with nausea. Another brother has alopecia areata. Her father recently died of a heart attack. Her mother, who is still living, has

occasional headaches The patient remembers no illness except shingles Her general physical condition is excellent Her bowel movements and her menstrual periods are normal She is moderately obese (height $5\frac{1}{2}$ feet [167.6 cm], weight 167 pounds [75.7 Kg]) On March 4, 1940 examination at the Lahey Clinic revealed nothing of importance A roentgenographic examination of the gastrointestinal tract was made there On May 28, 1941 I referred her to the Massachusetts General Hospital, where a thorough physical examination showed nothing abnormal A Hinton test gave a negative reaction The basal metabolic rate was $+4$ per cent

On Nov 27, 1940 I referred her to Dr G Colket Caner for a neurologic examination Aside from the ocular condition, his findings were normal While she was in the esophoric phase of an attack he subjected her, at my suggestion, to a prostigmine test His report follows

"After subcutaneous injection of 2 cc of a 1:2,000 solution of prostigmine methylsulfate and 1/100 gram (0.6 mg) of atropine sulfate, the patient complained that she was not able to swallow, became extremely apprehensive and presented multiple peculiar somatic symptoms Probably the feeling that she could not swallow was due to a spasm of her pharynx or esophagus, for twitching soon developed in all muscles, an occasional reaction in normal persons after injection of prostigmine

"In addition to what seemed an hysterical reaction to the muscle spasms and twitchings produced by the prostigmine, the patient reacted in a neurotic way to the pain of the injection itself In spite of all this, however, it is hard for me to believe that the ocular symptoms have a psychic origin The result of the prostigmine test rules out myasthenia gravis" I may add that the injection had no effect on the esotropia

In October 1941 I referred the patient to Dr William G Lennox for examination, with special reference to epilepsy and migraine Excerpts from his reports follow

"In addition to the major symptoms (headache, migraine, strabismus), she had a sensation of her nose being blocked and of a 'cool chill blowing through [her] face' Presumably, this was paresthesia There was also sometimes a 'dead feeling' in one arm, a sensation as though the 'muscles were not right' This numbness might occur in either arm There was also some trouble with her leg, which she failed to describe accurately She did not complain of such sympathetic symptoms as flushing, chilliness and desire to urinate She had taken no medication because of a prejudice against it, which was familial

"The patient resembled her father in having a driving temperament She was ambitious, conscientious, sensitive and easily upset emotionally, although her external appearance was placid Although I did not go deeply into this aspect, she had the characteristics which are described as making up the migraine personality

"The electroencephalogram was entirely normal This is consistent with other cases of migraine in my experience, in which there is no personal or family evidence of epilepsy The dead feeling which she had in her arm suggested a more extensive pathophysiologic condition

"The patient let one of her full blown attacks pass without notifying me, but she came in the other day when she was having mild pain in the eye and symptoms suggestive of approaching strabismus Her electroencephalogram was again entirely normal

"I gave her 0.5 mg of ergonovine subcutaneously and after an hour 0.4 mg of ergonovine malleate intravenously This treatment did not seem to influence the pain Therefore, one must say either that she is one of the 10 per cent of patients with migraine who are not helped by ergot or that her headaches are not of the migraine type The test was not fully conclusive because she was not having a full blown attack"

As possible causes of the ocular attacks in this case, neoplasm, multiple sclerosis, syphilis and various infectious processes are excluded by the frequency and the relatively short duration of the attacks and, above all, by the fact that in the seven and a half years since their onset no other neurologic symptoms have developed Myasthenia gravis was excluded by the result of the prostigmine test Hysteria seems to be eliminated by the presence of orthophoria between the attacks, and by the fact that without exophoria no one can voluntarily diverge the eyes Moreover, the patient was not more emotionally unstable than most women of her age and race who are subject to migraine, and the attacks were not preceded by emotional distress Epilepsy, remotely possible as a cause, was excluded by the electroencephalograms

The only reasonable cause of the attacks seems to be migraine Since this disease is conspicuously hereditary, it is of considerable significance that a brother of the patient was subject to frequent attacks of severe migraine That another

brother had alopecia areata may also be of importance. But most significant is the fact that at the onset of each attack the patient had unilateral headache and other symptoms consistent with migraine and unexplained by any other cause.

The question now arises as to how migraine could produce such ocular attacks. In rare cases migraine causes transient paresis of one ocular nerve, almost always the third. The attacks may not always be associated with headache, and repeated attacks may result in permanent paresis of the affected muscles. In the present case, however, the ocular deviation was not paretic, and certainly was not dependent on involvement of one nerve alone. There are worthy of consideration, it seems to me, only three possible ways in which migraine could have caused the exophoric phase of the attacks in this case.

1 A vasomotor disturbance in the region of the nuclei of the sixth nerves might have caused hypertonia of these nuclei. Presumably, this would cause inhibition of the internal rectus muscles. As a result, exophoria with some limitation of inward motion, would be expected. Concomitance of conjugate motion probably would not be greatly affected. The near point of convergence would no doubt recede, but to just how great an extent cannot be predicted because nothing is definitely known as to what determines the limit of normal convergence.

2 A vasomotor disturbance, probably vasoconstriction, might have reduced the tonus of the nuclei supplying both internal rectus muscles. Presumably, this would reduce the inhibition of the external rectus muscles and produce results comparable to those mentioned in 1.

3 A vasomotor disturbance might have affected the convergent mechanism. Little is known about this mechanism, but the evidence for Perlia's nucleus as a convergence center is strong. On the other hand, the evidence for a divergence center is weak. It consists chiefly of the occurrence of a condition known as divergent paralysis. However, one can explain this condition more satisfactorily, it seems to me, by not assuming the existence of a divergence center. But even if the existence of such a center is assumed, the fact that convergence was so slightly limited would seem to exclude divergence spasm as the cause of the exophoric phase in the present case. When bifixation has been in disuse for a considerable period, concomitant exotropia, often of high degree, develops. It does so despite the fact that to some extent stimulation to convergence continues through its association with accommodation. Presumably, therefore, the convergence mechanism contributes to the internal rectus muscle a tonus removal of which, together with the corresponding inhibition of the external rectus muscle, permits the eyes to diverge. Hence it seems probable that a vasomotor disturbance in the region of Perlia's nucleus could reduce its tonus sufficiently to produce concomitant exotropia of 40 prism diopters. Whether or not sufficient convergence innervation could be sent from the cortex to restore this tonus and, in addition, make possible convergence of the eyes to 15 cm is problematic. However, it seems probable especially if, as I believe, the limit of convergence is normally imposed by the degree of inhibition of the antagonists. Moreover, in many cases of exotropia of 40 prism diopters the patient can converge his eyes to 15 cm.

The second of the aforementioned possible causes for the exophoric phase of the attacks would seem to be more probable than the first because migraine has seldom been known to affect even one external rectus muscle and because so far as has been observed, it depresses the activity of the ocular muscles it affects. The third possibility seems the most probable of the three because the vasomotor disturbance would need not only to be depressive but to involve a smaller area and would affect both eyes equally.

On the basis of the preceding explanation for the exophoric phase the esophoric phase is easily accounted for, which makes the whole explanation still more probable. The esophoric phase cannot have been caused by so-called divergence paralysis, because in this phase the near point of convergence was brought nearer to not farther from, the eyes. It could be explained on the assumption that a convergence spasm resulted from the great effort required to overcome the preceding exotropia or on the assumption that an excitatory state in Perlia's nucleus occurred as a rebound from the state of depression. The second assumption seems the more probable because the esotropia was not accompanied by miosis or by spasm of accommodation. It is to be noted that this explanation of the esophoric phase accords with the fact that the esotropia was always far less severe than the preceding exotropia. The instability of the muscle balance in the interphase is satisfactorily explained by the transition from the assumed depressed to the excitatory states in Perlia's nucleus.

Possibly the conditions described would result from a vasomotor disturbance in the region of a cortical center for convergence. The facts, however, that Perlia's nucleus is practically continuous with the nuclei of the third nerve and that ophthalmoplegic migraine almost exclusively involves the third nerve make it more reasonable to assume that it was Perlia's nucleus which was affected in the present case. If it was true, as the patient stated, that in one attack esotropia was not preceded by exotropia, it would seem that migraine can cause hypertonus of Perlia's nucleus without first depressing it. If future investigations should prove that Perlia's nucleus is not part of the convergence mechanism it would become necessary to assume that some unknown region concerned with convergence was affected in the present case.

I assume that both the sensory and the motor phenomena associated with migraine are due to localized vasomotor disturbances in the brain. That the sensory phenomena have this cause I have not the slightest doubt. Recently I examined sections of the occipital lobe of 1 of my patients, subject to migrainous scintillating scotoma, who thirty-one years before his death had suddenly acquired a permanent peripheral scotoma, similar in the two eyes. The sections showed a localized lesion which evidently was produced originally by necrosis and which so far as could be determined, corresponded to the scotoma. Other explanations have been advanced for the oculomotor paresis of migraine, notably, pressure on the affected nerve by a temporarily swollen hypophysis or by a temporarily distended large vessel. These explanations seem unlikely in view of the fact that they are not applicable to the sensory phenomena. The present case makes them still more improbable since the lesion in this instance could not have been peripheral.

SUMMARY AND CONCLUSIONS

In the case reported there occurred periodically nonparetic severe exotropia or exophoria, followed by transient esotropia. The exophoric and the esophoric phase of an attack each persisted about one week. At the onset of each attack the patient had severe headache, nausea and other symptoms consistent with migraine and not explained by any other cause.

It is safe to conclude that these remarkable oculomotor phenomena were produced by a recurring disturbance situated not farther peripheral than the midbrain and dependent on migraine, not hysteria.

The attacks seem best to be explained by the assumption that a vasomotor disturbance associated with migraine first depressed and then temporarily raised the tonus of Perlia's nucleus.

KERATOCONUS POSTICUS CIRCUMSCRIPTUS

IRVING H LEOPOLD, M D

PHILADELPHIA

Among the rare forms of corneal abnormalities, there exists a group characterized by anomalies of curvature of the posterior corneal surface. Butler has named and described two types of abnormal posterior corneal curvature. One form is called keratoconus posticus and is characterized by a perfectly regular and unusually short radius of curvature for the entire posterior corneal surface. The other form, called keratoconus posticus circumscriptus, shows a localized area of increased curvature on the posterior corneal surface. In both types the anterior corneal curvature is smooth, regular and of average radius. In both types the cornea is thinned in the area of increased curvature. This thinning involves the entire cornea in the first, or keratoconus posticus, type and is limited to a circumscribed area in the second type.¹

Stallard,² in 1930, reported the first case of so-called keratoconus posticus circumscriptus. Butler^{2b} and Ingram³ each recorded a case. All these reports have appeared in the English literature, evidently no case has been recorded in the American journals.

REPORT OF A CASE

A Negress aged 36 reported to the ophthalmologic clinic of the Hospital of the University of Pennsylvania, desiring a refraction, having recently broken her glasses. As far as she recalled, there had never been any injury to or inflammation of either of her eyes. However, she has always been aware of poorer vision in her left eye. She had been wearing glasses for ten years. Visual acuity without correction was 6/9 + 4 in the right eye and 6/60 in the left eye, with the best correction after cycloplegic examination it was 6/5 in the right eye and 6/30 in the left eye. External examination revealed nothing unusual concerning the lids, fissure or conjunctiva of either eye. The cornea of the right eye was clear and sensitive, with no irregularities, staining or opacities. The cornea of the left eye showed a slight, circumscribed haze at approximately 7 o'clock, just below the central area. The corneal reflex was present to a wisp of cotton, and the cornea did not stain with fluorescein. Intraocular tension was 20 mm of mercury in each eye, measured with a Schiötz tonometer. The pupils were equal and regular. They reacted equally and promptly, with good amplitude, to direct and indirect stimulation with light and to a near stimulus. Ocular movements were full, both for disjunctive and for conjugate movements. The cover test revealed only slight exophoria for near vision and orthophoria for distance. The lacrimal sacs were both free from discharge, and the nasolacrimal ducts were patent.

Slit lamp examination of the right eye revealed nothing pathologic. Examination of the left eye by sclerotic scatter (figure A) revealed a circumscribed, horizontally oval haze lying nasally just below the central area of the cornea. Most of the opacity as seen in optical section (figure B) lay in the posterior portion, and a definite thinning existed in this area. The cornea here was approximately one-half the thickness of the rest of the cornea. The anterior surface of the cornea was smooth and possessed the same curvature throughout, with no irregularity in the area of the lesion. The posterior radius of curvature, in the area of the lesion, was notably shortened. This curvature was not regular, but was most pronounced in

From the Department of Ophthalmology, Hospital of University of Pennsylvania

1 Butler, T H (a) Keratoconus Posticus, Tr Ophth Soc U Kingdom 50 551, 1930, (b) Two Rare Corneal Conditions, Brit J Ophth 16 31, 1932, (c) Discussion of the Rarer Forms of Keratitis, Tr Ophth Soc U Kingdom 57 32, 1937

2 Stallard, in discussion on Butler^{1a}

3 Ingram, H V Keratoconus Posticus, Tr Ophth Soc U Kingdom 56 263, 1936

the lower portion. No pigmentation could be seen on the posterior corneal surface, nor was an aqueous flare seen. Both the lens and the iris failed to reveal any signs of trauma or disease.

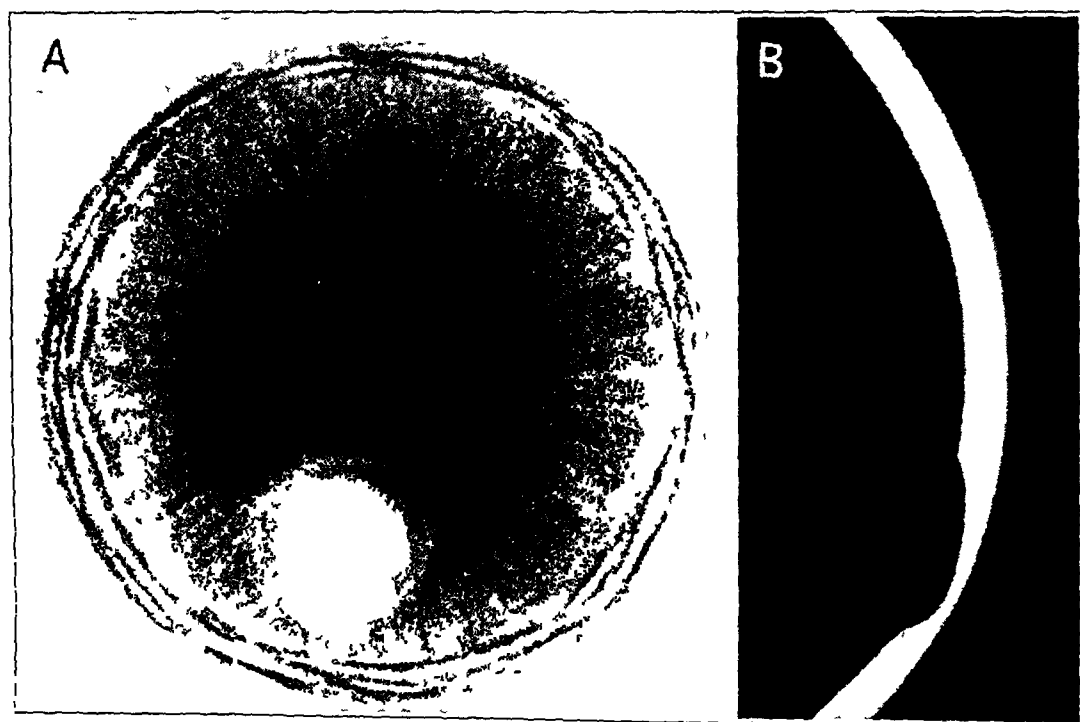
After instillation of 8 drops of 2 per cent homatropine hydrobromide, refraction with post-cycloplegic examination revealed 6/5 vision in the right eye, with a correction of +25 D sph, \ominus +25 D cyl, axis 160, and 6/30 vision in the left eye, with a correction of +2.00 D cyl, axis 5. A pinhole disk failed to improve vision in the left eye.

Ophthalmoscopic examination revealed no pathologic process, although the view of the left fundus was slightly hazy, as is usual in an astigmatic eye. Inspection of the visual fields revealed no scotomas.

Placido's rings appeared circular, and keratometric reflections were regular.

COMMENT

The signs observed in this case entitle the condition to be classed as a type of circumscribed posterior keratoconus. The failure to obtain improved vision in



A, corneal haze, as seen by sclerotic scatter, *B*, optical section, showing increased posterior corneal curvature in the region of corneal haze, with a normal anterior curvature.

Summary of Reported Cases of Keratoconus Posticus Circumscriptus

Observer	History of Injury	Age, Yr	Visual Acuity	Refractive Error	Position of Lesion	Sex
Stallard	+	Middle aged	6/24		Central	M
Butler	+	29	6/12 (1930) 6/9 (1931)	+2 D cyl, axis 30 -2 D cyl, axis 180	Not quite central	M
Ingram	-	54	6/60	Could not be improved	Central	F
Present case	-	36	6/30	+2 D cyl, axis 5	Not quite central	F

the left eye may be the result of amblyopia ex anopsia following uncorrected anisometropia of childhood.

The cases reported in the literature are indicated in the accompanying table.

In 2 of the cases reported there was a history of injury and in 2 there was none. No one actually saw this condition develop after an injury in a healthy cornea. So at best, the assumption of a traumatic origin is *post hoc ergo propter hoc* reasoning and may suffer the fallacies of all such logic.

SUMMARY

A case of keratoconus posticus circumscriptus is presented. No history of preceding disease or injury could be elicited.

CLASSIFICATION OF EXPERIMENTAL CATARACTS IN THE RAT

RECENT OBSERVATIONS ON CATARACT ASSOCIATED WITH TRYPTOPHAN
DEFICIENCY AND WITH SOME OTHER EXPERIMENTAL CONDITIONS

WILHELM BUSCHKE, M D

BALTIMORE

Since the early observations by Erdheim¹ in 1906, on cataract associated with tetany in rats and those by A. Buschke,² in 1913, on cataract produced by thallium, cataract has been observed with seven other experimental conditions of the rat. Such cataracts do not include the acute reversible opacities of the lens due to osmotic and physical factors. The question arises whether this fairly large body of experimental observations can be put to any use in solution of the problem of the pathogenesis of cataract. The occurrence of cataract in one species under a great number of different conditions appears to be a fortunate situation from the standpoint of comparative pathology.

Valuable information can be obtained by systematic studies with the slit lamp during the early stages and throughout the development of the cataract and by observation on allied manifestations elsewhere in the body. On the basis of such observations, Goldmann³ differentiated thallium cataract and tetanic cataract and showed that the former cannot be explained by an insufficiency of the parathyroids. Observations on the allied symptoms of galactose cataract have led other authors⁴ to suspect the relation of this cataract to osmotic disturbances. Similar observations, which include studies of the other experimental cataracts in the rat, permit a

From the Wilmer Ophthalmological Institute of the Johns Hopkins University School of Medicine

This work was supported in part by grants for the study of amino acids in nutrition made by the Rockefeller Foundation, Merck & Company, Inc., Eli Lilly and Company, and E. R. Squibb & Sons to the Department of Pediatrics, Johns Hopkins University School of Medicine. The work on riboflavin deficiency and on galactose and xylose cataracts, briefly referred to in this paper, is being carried on under grants from the John and Mary R. Markle Foundation.

The observations on tryptophan-deficient rats reported in this paper are part of a general study on the clinical and chemical changes occurring in amino acid deficiencies in experimental animals and in human beings. This study was conducted in the department of pediatrics of the Johns Hopkins Hospital and University and was under the immediate direction of Dr. L. Emmett Holt, Jr. The participation of the department of ophthalmology in the study was incidental and was made at the specific invitation of Dr. Holt. Full reports of the study as a whole will be made by Dr. Holt and his co-workers in other journals. The observations reported here are, however, of special ophthalmologic interest and on this account appear to warrant a separate report in the ophthalmologic literature.

The cataracts in rats with experimental diabetes occurred in the course of studies conducted by Dr. Curt P. Richter in the psychobiologic laboratory of the Phipps Psychiatric Clinic, Johns Hopkins Hospital, who also observed the cataracts. Dr. Richter permitted me to study these eyes. Reference to these studies is made by permission of Dr. Richter.

1 Erdheim, J. *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **16** 632, 1906.

2 Buschke, A. *Arch. f. Dermat. u. Syph.* **116** 477, 1913.

3 Goldmann, H. *Arch. f. Ophth.* **122** 146, 1928.

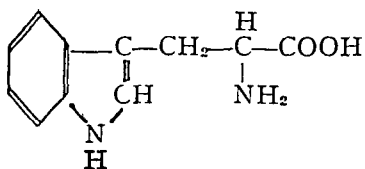
4 (a) Sullmann, H., and Weekers, R. *Ztschr. f. Augenh.* **95** 58, 1938. (b) Bellows, J. G., and Chinn, H. *Theories of Cataract*, *Arch. Ophth.* **26** 1066 (June) 1941.

classification of these cataracts into three fairly well circumscribed groups, the diabetic, the tetanic and the dystrophic

In the present study, in addition to the cataracts associated with tryptophan deficiency and with experimental diabetes, some observations have been made on riboflavin-deficient rats and on the cataracts due to galactose and xylose. As a result of these comparative studies, a classification of experimental cataracts is made, with the object of delimiting the individual groups of cataract.

OBSERVATIONS ON TRYPTOPHAN-DEFICIENT RATS

Tryptophan is an indole aminopropionic acid and has the following structure



It can be replaced in the diet only by a few other indole compounds, e. g., indole pyruvic acid. It has been known for many years that the absence of tryptophan from the diet results in the arrest of body growth of young animals.⁵ In addition, some specific manifestations of the deficiency have been observed. In rats with experimental tryptophan deficiency, blindness with opacities in the ocular media was noted by Curtis, Hauge and Kraybill,⁶ and the occurrence of cataract and vascularization of the cornea in this condition was reported by Totter and Day.⁷

In the present study, attention has been especially directed toward the morphologic character and mode of development of tryptophan deficiency cataract and its association with lesions in certain other organs.

MATERIAL AND METHODS

Both albino and hooded rats were used by Dr. Holt and Dr. A. A. Albanese in their experiments. The rats belonged to two strains, of which one was bred as a mixed strain in the laboratory of the department of pediatrics and the other was an unidentified strain and had been obtained by Dr. Albanese from an out-of-state source.

The dietary study was carried out as a "paired feeding" experiment, i. e., the food intake of the control animals was restricted to that of the deficient animals of the same age in order to rule out inanition as a possible cause of symptoms. The diet used by Dr. Holt and Dr. Albanese was compounded as follows: protein (acid-hydrolyzed casein concentrate), 147 Gm., l-cystine, 15 Gm., sucrose, 150 Gm., starch, 420 Gm., agar, 20 Gm., salt mixture (see next paragraph), 20 Gm., hydrogenated cottonseed oil (Crisco), 190 Gm., brewers' yeast (Mead Johnson), 427 Gm., Mead Johnson's cod liver oil substitute,^{7a} 50 Gm., and water to make the proper consistency.

The salt mixture used had the following composition: sodium chloride, 189 Gm., dicalcium phosphate, anhydrous, 25 Gm., magnesium sulfate, anhydrous, 6.86 Gm., potassium bicarbonate, 44.4 Gm., potassium chloride, anhydrous, 2.88 Gm., ferric citrate U. S. P., 2.21 Gm., cupric sulfate, anhydrous, 0.24 Gm., manganese sulfate, anhydrous, 0.15 Gm., potassium iodide, 0.015 Gm., and sodium fluoride, 0.03 Gm.

The diet of the control animals was exactly like that of the deficient animals except for the supplementation with 2.25 Gm. of tryptophan per thousand grams of food.

In the first series of their experiment, in which were made most of the observations reported here, 8 animals of about 100 Gm. body weight were placed on the deficiency diet.

⁵ Berg, C. P., Rose, W. C., and Marvel, C. S., *J. Biol. Chem.* **85**, 207 and 219, 1929; Jackson, R. W., *ibid.* **73**, 523, 1927, **84**, 1, 1929.

⁶ (a) Curtis, P. B., Hauge, S. M., and Kraybill, H. R., *J. Nutrition* **5**, 503, 1932; (b) Berg, C. P., and Potgieter, cited by Totter and Day.⁷

⁷ Totter, J. R., and Day, P. L., (a) *J. Biol. Chem.* **140**, cxxxiv, 1941, (b) *J. Nutrition* **24**, 159, 1942.

^{7a} The substitute contains fish liver oil, sardine oil and maize oil plus viosterol.

and a corresponding number on the control diet. In addition, 4 adult albino rats of between 200 and 300 Gm were placed on the deficiency diet.

In addition to this series, observations were made on the eyes of a larger series (over 30) of similarly deficient and control rats. These rats, however, were killed at various times during the experiment to provide material for the study of the systemic lesions. Systematic observations on the eyes of these animals were therefore not possible. In general, the cataractous and corneal changes observed were the same as those systematically studied in the first series. Reference will later occasionally be made to this larger series.

The animals were examined with the slit lamp about once a week, with the use of atropine mydriasis, and during the development of the cataracts they were examined every day.

For slit lamp observation the rats were examined on a stand, as shown in figure 1. For slit lamp drawings the rats were immobilized by subcutaneous injection of 0.25 cc per hundred grams of body weight of a 1:10 dilution of a commercial bulbocapnine solution.⁸

TRYPTOPHAN DEFICIENCY CATARACT

This type of cataract has been observed only in young rats, never in adults. It occurs in two morphologically distinct forms, the acute and the chronic.

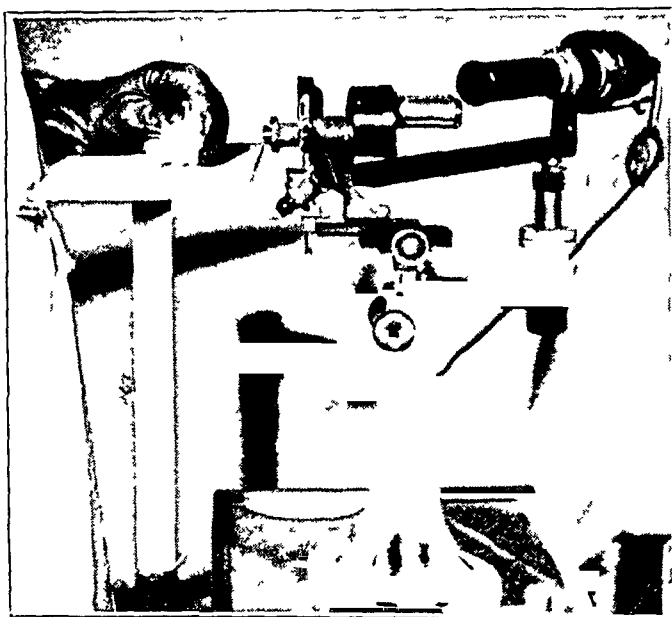


Fig 1—Slit lamp examination of the rat's eye

Acute Type of Cataract—The acute type was observed in 3 of 4 young animals all of the same strain. The general pathologic picture was as follows:

Seven to eleven weeks after the animal was placed on the deficient diet, a feathery opacity, with leaflike margins, developed in the posterior subcapsular cortex. The suture lines were clearly visible and gaped slightly, and some medium-sized vacuoles were visible along the suture lines. The final opacity was somewhat denser at the peripheral margins than at the posterior pole of the lens (fig 2 A and B).

While the opacities in the posterior cortex were developing, the anterior cortex and the nucleus remained clear. After the development of the posterior opacity short, spokelike opacities appeared in the anterior cortex near the equator, followed within four days by the development of a shell-like, perinuclear opacity. This consisted of innumerable fine motes, which gave a grayish, milky appearance to the anterior cortex (fig 2 C and D). The nucleus now rapidly became opaque.

⁸ Richter, C. P., and Paterson, A. S. *J. Pharmacol. & Exper. Therap.* **43**: 677, 1931.

and the perinuclear opaque zone became wider. The anterior suture lines gaped to become narrower again as the cataract became mature (fig 2 *E* and *F*). The cataract became mature within three weeks after the onset of the first changes.

Chronic Type of Cataract—This type of cataract was seen in 3 of 4 animals of one strain and in 1 of the other strain. The general pathologic picture was as follows:

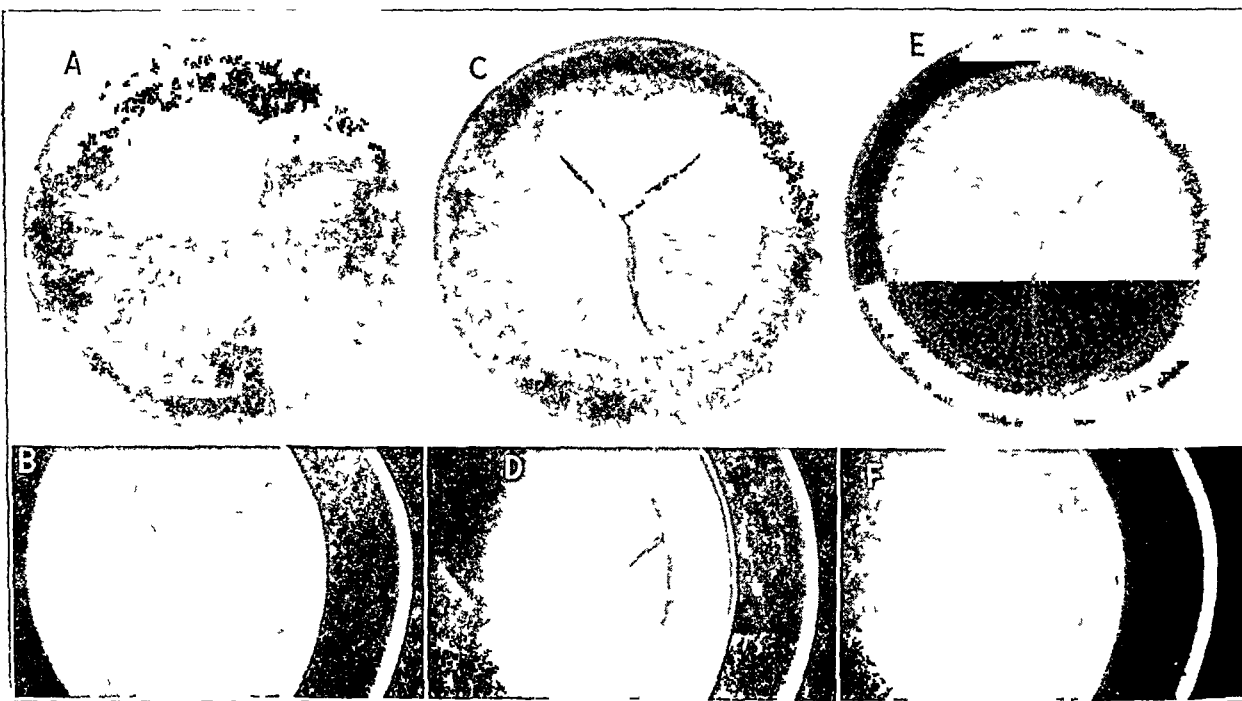


Fig 2—Cataract associated with acute tryptophan deficiency. *A*, composite drawing of the posterior cortex and, *B*, optical section in the first stage. *C*, composite drawing of the posterior cortex and, *D*, optical section in the second stage. *E*, composite drawing of the posterior cortex and, *F*, optical section in the third stage.

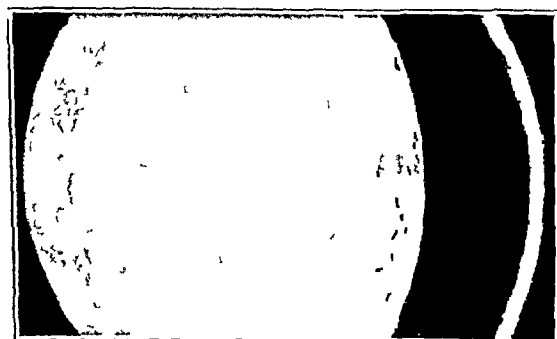


Fig 3—Optical section in a case of tryptophan deficiency cataract, chronic form, in the rat.

Eight to ten weeks after the rat was placed on the tryptophan-deficient diet hazy opacities appeared along the anterior subcapsular suture lines, and the feathery structure of the superficial cortex became visible. Fine, dotted opacities appeared in the superficial portion of the cortex. During the following weeks a fine network of cobweb-like opacities developed in the anterior and the posterior superficial portions of the cortex (fig 3) and this zone of opacities gradually

gained in depth. Occasionally a few fine vacuoles were visible in this zone. The deep cortex and the nucleus remained clear, and the cataract did not mature during the lifetime of the animal, i. e., within three to nine weeks after the onset of the first changes.

In 1 rat a combination of the acute and the chronic type of cataract was seen. In this animal cobweb-like opacities appeared in the superficial cortex, and a flat, dense, leaflike opacity developed around the posterior pole of the lens. Within six to eight weeks after the onset of the first changes, perinuclear and nuclear opacities developed in one eye, and the feathery arrangement of the fine superficial cortical opacities became clearly visible. The suture lines gaped. However, the cataract in the other eye did not progress beyond the stage of the posterior polar opacity (fig. 4).

Arrest of the Acute Cataract by Supplementation of the Diet with Tryptophan — To 1 animal, tryptophan was supplied at the time that the leaflike opacity had developed in the posterior subcapsular region of the lens in one eye.

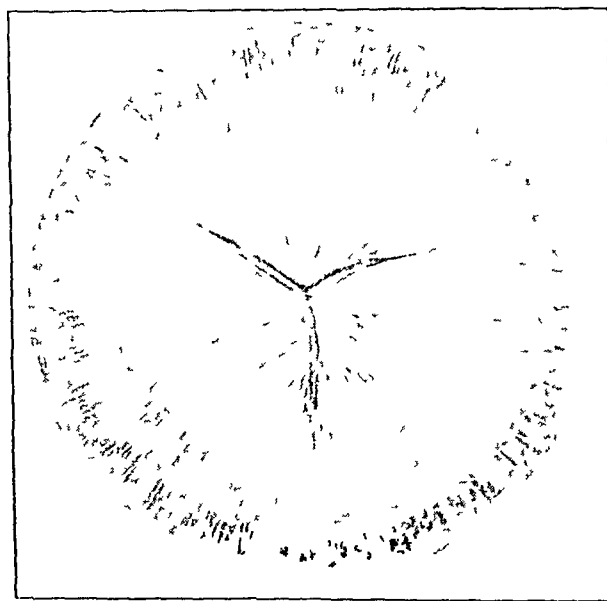


Fig. 4—Composite drawing of tryptophan deficiency cataract, combined form, in the rat.

During the first five weeks after the supplementation of the diet, some snowflake opacities appeared around the nuclear suture lines, and in one eye a flat, rosette-like opacity developed at the anterior nuclear surface (fig. 5 A). However, the cataracts did not progress further, and even during these first five weeks after supplementation of the diet a clear subcapsular zone of fresh lens substance was deposited around the optically denser deep portion of the cortex. This clear superficial zone was separated from the deeper cortex by a dense zone of discontinuity (fig. 5 B). In the following months the clear superficial zone became gradually wider and produced the picture of a lens within a lens.

It is of interest that when tryptophan was administered to a deficient animal some further opacities of the lens developed even though the general condition of the rat had begun to improve and the animal had started to gain weight. It is evident that some latent, irreparable damage to the lens fibers had taken place already and led eventually to manifest opacities. Similar phenomena are well

known in the realm of injuries due to actinic rays and have been reported also in cases of tetanic⁸ and of galactose cataract⁹

Histologic Studies—In the cataractous lens, globular degeneration of the lens fibers, particularly in the superficial cortex, was noted. In addition, pronounced proliferation of the epithelium was seen in the cataract complicating acute tryptophan deficiency.

Histochemical Tests for the Presence of Bound Indoles—Tryptophan and other indoles form colored products in the presence of aldehydes. Tryptophan must be split off by hydrolysis from the protein molecule before it gives this reaction.

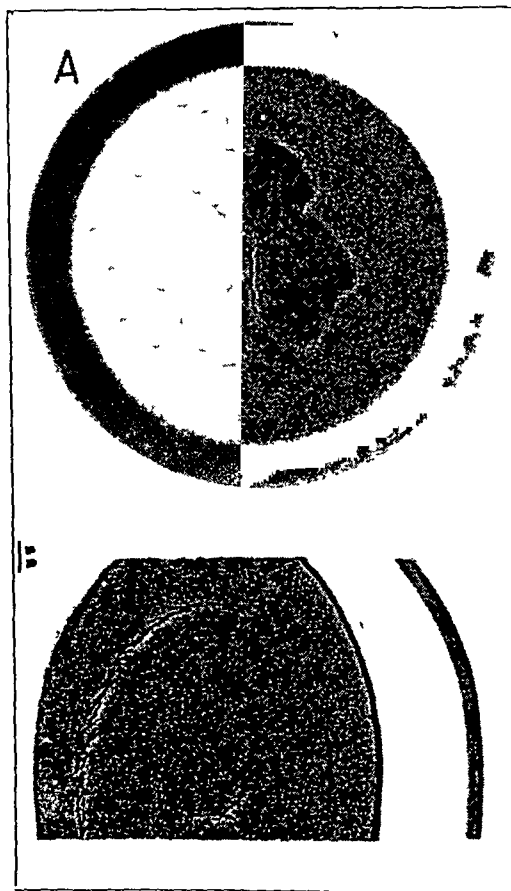


Fig 5—*A*, composite drawing, and, *B*, optical section (other lens), of tryptophan deficiency cataract arrested by supplementation of the diet with tryptophan.

The reagents employed in the test are (1) the vanillin reagent, consisting of a 1 per cent solution of vanillin in 50 per cent hydrochloric acid, (2) concentrated hydrochloric acid, and (3) 3 per cent hydrogen peroxide.

Method—Paraffin sections of material fixed in solution of formaldehyde U S P are deparaffinized, carried through the alcohols to water and dried between filter paper. One drop of concentrated hydrochloric acid is placed on the section and left there about one-half minute. One drop of the vanillin reagent is added without the sections being washed, and one-half minute later 1 drop of 3 per cent hydrogen peroxide is added. After some minutes the fluid is drained off with filter paper, and the preparation is washed with distilled water. It can then be carried through the alcohols and xylene and mounted in Canada balsam. A qualitatively positive reaction is an intensely red color.

⁹ Darby, W. J., and Day, P. L. *J Biol Chem* **133** 505, 1940.

The histochemical test for bound indole, presumably tryptophan, in the cataractous lens of the tryptophan-deficient rat still gives a definitely positive reaction, even in the advanced stages of cataract. Sometimes the reaction is slightly weaker than that in the control lenses, particularly in the cortex of the lens, but it has never been negative. The result indicates that even in the advanced stages of tryptophan deficiency cataract no complete loss of bound indole from the proteins of the lens has taken place. This method, however, does not lend itself to quantitative conclusions.

Changes in the Lens in Control Animals—The control animals were not maintained on a normal stock diet but received the same diet as the tryptophan-deficient animals supplemented only with tryptophan, and the quantity was restricted to the food intake of the deficient rats.

In some of the control rats there developed minor changes in the lens which deserve special description. The most important lesions were abnormally visible deep cortical zones of discontinuity or thin zonular opacities. The changes could not have been detected with an ophthalmoscope alone and were visible only with the slit lamp.

In order to find out whether these lesions might be strain-specific, endogenous changes in the lens, 31 rats of the same strain aged from 3 to about 6½ months which had been kept on unlimited stock diet were examined. Of these normal rats, only 1 showed a circumscribed reflecting zone in the deep cortex.

It is thus likely that the zonular changes seen in some of the rats on a tryptophan control diet did not represent a hereditary type of lesion but, rather, were due to some exogenous damage associated with the difference between the tryptophan control diet and the ordinary stock diet. The tryptophan control diet was not sufficiently inadequate in regard to quality and quantity to produce progressive cataract or damage to the lens of such magnitude that it could not be overcome during the later growth of the lens. However, the control diet may have exerted a transitory influence on the lens at an early period which was "outgrown" later by the normal growth of the lens from the periphery.

It is possible that the lens-damaging factor or factors intrinsic to the tryptophan control diet predisposed to manifestations of damage to the lens encountered in the rats on the tryptophan-deficient diet. It is not known which factor or factors these were. Some connection with the quantitative restriction of the diet, as used in the paired feeding technic, is possible.

LESIONS ASSOCIATED WITH TRYPTOPHAN DEFICIENCY CATARACT

Changes in the Cornea—Vascularization of the cornea and keratitis were observed in tryptophan-deficient rats by Totter and Day.⁷ In the tryptophan-deficient animals of Dr. Albanese and Dr. Holt, vascularization of the cornea was seen with the slit lamp in 6 of 8 of the young rats in the first series and in the majority of the rats of the second series. In some rats weighing 40 Gm. at the time they were placed on the deficient diet, vascularization was seen within ten days. It also occurred in adult rats receiving the deficient diet. In general, the vascularization of the cornea in the young rats was well advanced by the time the cataract developed. Narrowing of the corneal vessels to invisibility was observed on examination with the slit lamp within a few weeks after supplementation of the diet with tryptophan. None of the control animals in the paired feeding experiments showed this vascularization.

On examination with the slit lamp the vessels appeared as predominantly superficial loops originating in the superficial perilimbal plexus (fig 6). Often fine, straight sprouts arose from the vertex of a capillary loop and ran in a radial direction. Under a high power lens circulation of the blood could be seen in the wider loops.

Study of flat preparations of the cornea after injection of india ink (method of Bessey and Wolbach¹⁰) showed under a higher power lens, that the fine sprouts arising from larger capillary loops finally bent toward similar sprouts arising from another capillary loop (fig 7). Obviously, new capillary loops are formed in this way.

Infiltration of the cornea was seen in some eyes of tryptophan-deficient rats. It began sometimes around the vertex of capillary loops and in some cases the whole cornea became cloudy and "steamy." Occasionally, in advanced stages the surface of the cornea appeared dry.

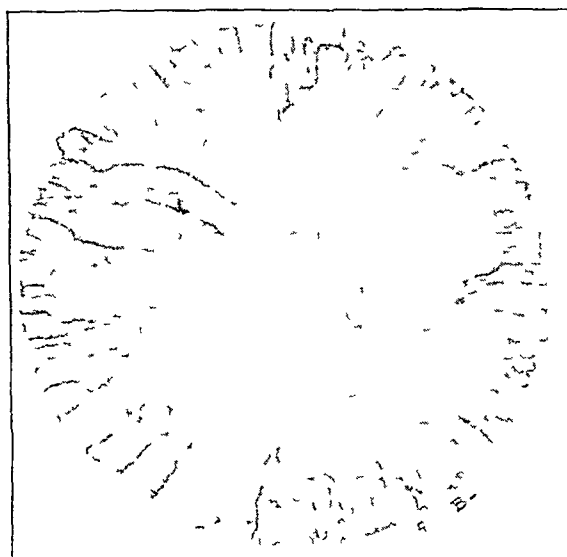


Fig 6—Vascularization of the cornea associated with tryptophan deficiency in the rat. Composite drawing with the slit lamp.

Histologic sections confirmed the predominantly superficial location of the capillaries (fig 8A); sometimes the epithelium was even elevated. In more advanced stages capillaries were also visible in the deeper layers of the stroma, together with polymorphonuclear and round cell infiltration (fig 8B).

For comparison, I have studied the corneal lesions associated with riboflavin deficiency.

The diet of the riboflavin-deficient rats was made up of Smaco, a vitamin B complex-free basal diet,^{10a} with the following supplements in the amounts stated per kilogram of basal diet: thiamine hydrochloride, 8 mg; pyridoxine hydrochloride, 12 mg; calcium pantothenate, 500 mg; choline chloride, 2,000 mg; nicotinic acid, 200 mg; and inositol, 200 mg. The diet of the control animals contained, in addition, 12 mg of riboflavin per kilogram of basal diet.

The corneas were examined with the slit lamp in flat preparations after injection of india ink and in histologic sections. On the basis of these studies, I can

10 Bessey, C. A. and Wolbach, S. B. *J. Exper. Med.* **69** 1, 1939.

10a The composition of the vitamin B complex-free diet was as follows: sucrose 68 per cent, vitamin-free casein 18 per cent, vegetable oil 8 per cent, salt mixture no. 2 U. S. P. 4 per cent, and cod liver oil 2 per cent.

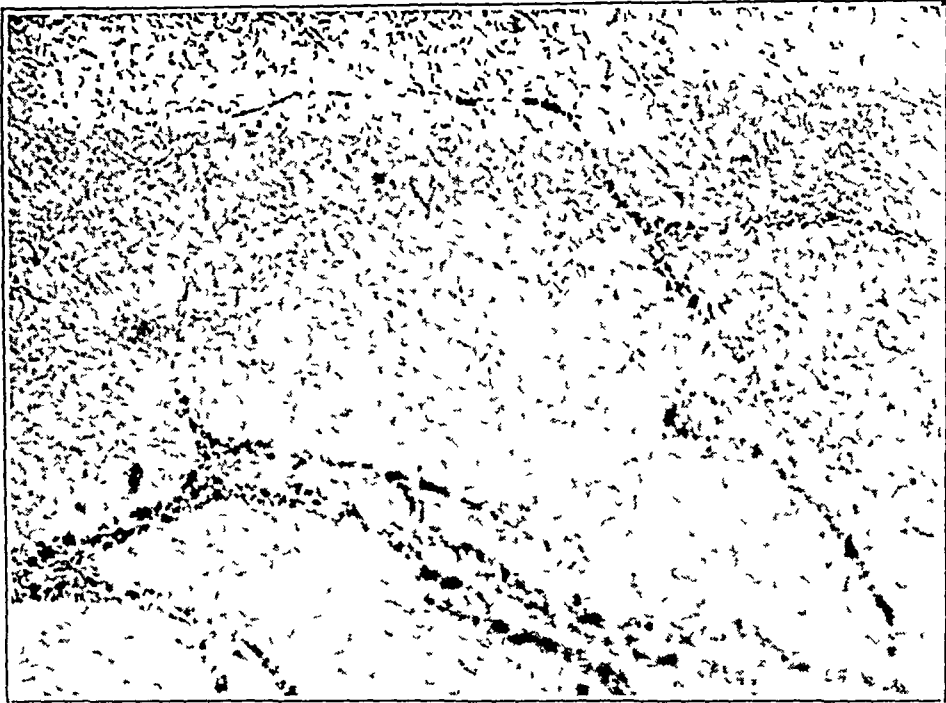


Fig 7—Photomicrograph showing vascularization of the cornea associated with tryptophan deficiency in the rat. Injection with india ink

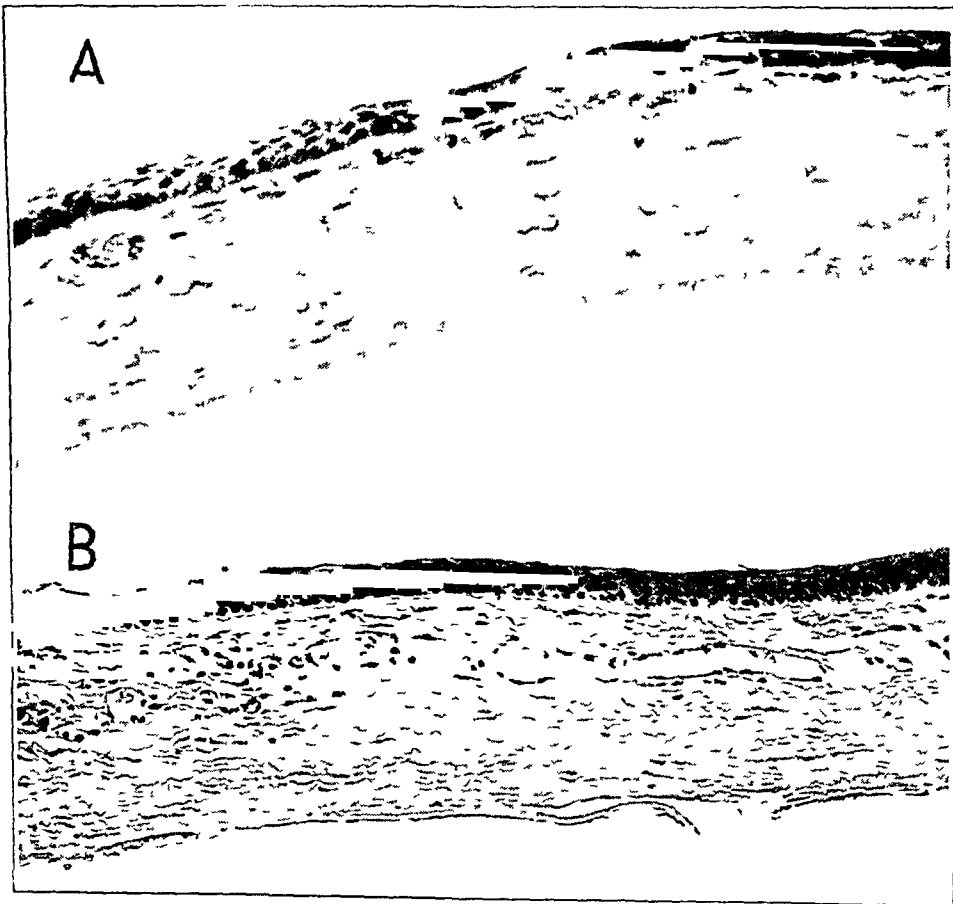


Fig 8—Photomicrographs showing corneal changes associated with tryptophan deficiency in the rat. *A*, subepithelial vascularization, *B*, vascularization and round cell infiltration. Hematoxylin and eosin stain

amply confirm the descriptions of earlier observers,¹¹ but, contrary to the reports of Totter and Day,⁷ I was unable to note any significant differences between the corneal lesions in the riboflavin-deficient and those in the tryptophan-deficient animals

*Arrest of Body Growth in Young Animals*⁵

*Alopecia and Other Cutaneous Lesions*¹²—These changes occurred both in young and in adult rats. Totter and Day,^{7b} using two different diets, observed cutaneous changes only with one of the diets. Predisposing dietary factors other than tryptophan deficiency may play a role here, too.

*Atrophy of the Testicles and Aspermatogenesis*¹³

*Lesions in the Incisor Teeth*¹⁴—It is to be noted that the rat's incisor teeth, like the lens, grow throughout life. The relation of lesions in these teeth to tryptophan deficiency, however, demands further study.

COMMENT

Relation of Ocular Lesions to Tryptophan Deficiency—Whether or not any of the manifestations are secondary to lesions elsewhere in the body cannot be decided. It is certain that not all the observed manifestations can be secondary to changes in the testicles because castration does not produce similar symptoms.

A secondary inanition deficiency due to diminished food intake is unlikely because the experiment was carried out as a paired feeding experiment, and none of the control animals manifested any of the forms of cataract observed in the tryptophan-deficient animals.

Likewise, "cold cataract"¹⁵ and "salt cataract,"¹⁶ which have been observed in very young rats on exposure of the eyes, can be ruled out because the cataracts described in this study occurred in rats of 100 Gm body weight and the opacities were not reversible and did not develop as rapidly as those seen in such cataracts.

The possible role of predisposing dietary factors other than tryptophan deficiency has already been discussed.

It is of interest that vascularization and infiltration of the cornea have been observed with a great variety of conditions: riboflavin deficiency,¹¹ thallium poisoning,¹⁷ vitamin A deficiency,¹⁸ zinc deficiency,¹⁹ sodium deficiency,²⁰ lysin deficiency^{7b} and deficiency of an unidentified factor of the vitamin B complex.²¹ Recent observations with the slit lamp on a highly inbred strain of rats suggest that vascularization of the cornea occurs also in certain strains of rats as a geno-

11 O'Brien, C. S. Experimental Cataract in Vitamin G Deficiency, *Arch Ophth* 8:880 (Dec) 1932. Eckhardt, R. E., and Johnson, L. V. Nutritional Cataract and Relation of Galactose to Appearance of Senile Suture Line in Rats, *ibid* 21:315 (Feb) 1939. Bessey and Wolbach.¹⁰

12 (a) Buschke, W., Albanese, A. A., and Follis, R. H., Jr. *Federation Proc* 1:175, 1942. (b) Albanese, A. A., and Buschke, W. *Science* 95:584, 1942. (c) Totter and Day.^{7b}

13 Shettles, L. B. *Proc Third Ann Conf Biol Spermatozoa*, 1942, p. 28.

14 Buschke, Albanese and Follis.^{12a} Albanese and Buschke.^{12b}

15 Goldschmidt, M. *Klin Wchnschr* 6:635, 1927.

16 Goldmann, H., and Rabinowitz, G. *Klin Monatsbl f Augenh* 81:771, 1928.

17 Ginsberg, S., and Buschke, A. *Klin Monatsbl f Augenh* 71:385, 1923.

18 Wolbach, S. B., and Howe, P. R. *J Exper Med* 42:753, 1925. Bessey and Wolbach.¹⁰

19 Follis, R. H., Jr., Day, H. G., and McCollum, E. V. *J Nutrition* 22:223, 1941.

20 Follis, R. H., Jr., Orent-Keiles, E., and McCollum, E. V. *Am J Path* 33:504, 1942.

21 G. G. G. G., Johnson, L. V., and Eckhardt, R. E., cited by Evans, E. A. *The Biological Action of the Vitamins*, Chicago, University of Chicago Press, 1942, pp. 64-65.

typical trait when the animals are receiving normal diets. Occasionally superficial blood vessels were seen in histologic sections of the cornea of old rats on normal diets, possibly as the result of trauma. Furthermore, examination of large numbers of stained flat preparations of the normal rat cornea not infrequently revealed fine capillaries in the peripheral stroma. While the latter changes are not comparable to the massive vascularization of the cornea in rats with tryptophan deficiency and in some other conditions, they signify that the rat cornea is particularly susceptible to vascularization, probably more so than the human.

Special Features of Tryptophan Deficiency Cataract—Tryptophan deficiency cataract showed an outspoken variability among the rats of one age group and one species. It occurred in at least two morphologically different forms—an acute and a chronic. This variability points to the importance of factors other than the experimental dietary deficiency alone in the development and shaping of this cataract.

Tryptophan deficiency cataract is associated with several manifestations which have some relation to growth activity—inhibition of body growth and manifestations in epithelial tissues, which (like the crystalline lens) continue to grow throughout life (hair, testicular epithelium). This points to the (direct or indirect) importance of tryptophan in the metabolism of these growing tissues. It may be noted in this connection that some indole compounds, chemically related to tryptophan, act as growth substances in plants (heteroauxins).²²

The presence of these features and the absence of certain characteristics of other types of cataract permit a comparison of tryptophan deficiency cataract and other experimental forms, which will be discussed in the next section.

CLASSIFICATION OF EXPERIMENTAL CATARACTS IN THE RAT

In the introduction, it was pointed out that studies of the development of cataract, as observed with the slit lamp, and of the allied manifestations elsewhere in the body may shed light on the pathogenic differentiation of experimental forms of cataract. In the present paper tryptophan deficiency cataract in the rat has been described from these points of view. It is of interest to compare these observations with those on other experimental cataracts in the same species.

In the accompanying table, the nine experimental cataracts of the rat thus far recognized have been classified on the basis of their morphologic and developmental features, as well as their allied manifestations. The three main groups of cataract in this classification are the diabetic, the tetanic and the dystrophic. Studies on cataracts of the diabetic group will be reported on later in more detail.

The table may be briefly discussed. Tryptophan deficiency cataract has in common with thallium cataract and with riboflavin deficiency cataract its outspoken variability and its association with inhibition of body growth and with manifestations in certain other organs, namely, the cornea, the skin and the testicles. The histopathologic changes in the skin associated with experimental riboflavin deficiency have been described by Sullivan and Nicholls,²³ and the observations in the testicles and other organs, by Shaw and Phillips.²⁴ The allied manifestations occurring with thallium poisoning have been reviewed by A. Buschke and Peiser.²⁵

Although some of the allied manifestations of this group of cataracts are observed also with tetanic cataract, the latter is characterized by the chemical changes

22 Kogl, F., Haagen-Smit, A. J., and Erxleben, H. *Ztschr. f. physiol. Chem.* **228** 90, 1934.

23 Sullivan, M., and Nicholls, J. *J. Invest. Dermat.* **4** 181, 1941.

24 Shaw, J. H., and Phillips, P. H. *J. Nutrition* **22** 345, 1941.

25 Buschke, A., and Peiser, B. *Ergebn. d. allg. Path. u. path. Anat.* **25** 1, 1931.

Literature Cataracts Observed in the Rat

Experimental Condition	Authors	Special Features of Cataract with Respect to Morphologic Features, Development and Occurrence	Allied Pathologic Manifestations
Diabetic Group			
Galactose cataract	Mitchell, H. S., and Dodge, W. M. <i>J. Nutrition</i> 9: 37, 1933; Mitchell, H. S. <i>ibid.</i> 12: 117, 1936; Proc. Soc. Exper. Biol. & Med. 41: 67, 1932; Yuckin, A. M., and Arnold, C. H. <i>Cataracts Produced in Albino Rats on Ration Containing High Proportion of Lactose or Galactose</i> , Arch. Ophth. 14: 960 (Dec.) 1935; Sullivan and Weckers, in Darby and Day's <i>Sasak</i> 286; Gifford, S. R., and Bellows, J. <i>Histologic Changes in Lens Produced by Galactose</i> , Arch. Ophth. 21: 916 (Feb.) 1911	Strong vacuolization in superficial cortex, particularly at equator of lens, in some stages (fig. 11 C)	Increased appetite, polydipsia, polyuria, high monosaccharide concentration in blood
Xylose cataract	Darby, W. I., and Day, P. L. <i>Proc. Soc. Exper. Biol. & Med.</i> 41: 67, 1936, footnote 9, present report	Strong vacuolization in superficial cortex, particularly at equator of lens (fig. 11 D)	Polydipsia, polyuria, high monosaccharide concentration in blood
Cataract accompanying postoperative diabetes (pancreatectomy)	Reichter, C. P., and Buschke, W. To be published elsewhere	Cataract has been observed in adult rats with strong vacuolization in superficial cortex and at equator in some stages (fig. 11 A and B)	Increased appetite, polydipsia, polyuria, high monosaccharide concentration in blood
Let milk Group			
Cataract associated with dietary tetany	von Buhr ^{4b}	Opacities appear in anterior superficial cortex in close correlation with attacks of tetany (manifest or latent)	Low calcium phosphate ratio in blood; neuromuscular hyperexcitability, lesions of incisor teeth
Cataract associated with postoperative tetany (parathyroidectomy)	Goldmann ⁹	Opacities appear in anterior superficial cortex in close correlation with attacks of tetany (manifest or latent) (fig. 10)	Low calcium phosphate ratio in blood; neuromuscular hyperexcitability, arrest of body growth, lesions of incisor teeth
Dystrophic Group			
Cataract due to chronic thallium poisoning	Buschke, A., Gushers, and Buschke ¹⁷ ; Donski, J. <i>Arch. f. Ophth.</i> 128: 201, 1932; Mamoli, L. <i>Ann. di ottal. e clin. ocul.</i> 75: 35, 1927; von Meilin, A. <i>Experimentelle Untersuchungen über die Entstehung des Thallium Stares nebst Bemerkungen über die neue vererbare und angeborene St.-form bei weissen Ratten</i> (Munich, K. Albertssoetter, 1926)	Cataract occurs only in growing rats; variability in occurrence; outspoken, cortical and nuclear (fig. 9)	Arrest of body growth, alopecia, vascularization of cornea, keratitis, alopecia and dermal lesions, atrophy of testicles, nerve lesions, endocrine lesions
Cataract associated with riboflavin deficiency	Day, P. L., Langston, W. C., and O'Brien, C. S. <i>Am. J. Ophth.</i> 14: 106, 1931; Day, P. L. <i>J. Nutrition</i> 12: 39, 1936; Day and Darby ¹⁸ ; Bourne, M. C., and Pyke, M. A. <i>ibid.</i> 29: 1865, 1935; Gyorgy, P. <i>ibid.</i> 29: 741, 1935; Cosgrove, R. W., and Day, P. L. <i>Am. J. Ophth.</i> 25: 544, 1942; Richardson, L. R., and Hogan, A. G. <i>Research Bull.</i> 241, Missouri Agricultural Experiment Station, 1936 cited by Bessey and Wolbach ¹⁹ ; Bessey and Wolbach ¹⁹ ; Baum, H. M., Michaelree, J. F., and Brown, E. B. <i>Science</i> 97: 24, 1942	Cataract occurs only in growing rats; variability in occurrence and morphologic character very outspoken, cortical and nuclear	Arrest of body growth, vascularization of cornea, keratitis, alopecia and dermal lesions, atrophy of testicles, nerve lesions, endocrine lesions
Cataract associated with tryptophan deficiency	Curtis, Hauge and Kraybill ²⁰ ; Berge and Potgieter ²¹ ; Toller and Day ²² ; Buschke, Albanese and Pollis ¹³ ; Albanese and Buschke ¹³ ; Present report	Cataract occurs only in growing rats; variability in occurrence and course of development; outspoken, cortical and nuclear	Arrest of body growth, vascularization of cornea, keratitis, alopecia and other cutaneous lesions, atrophy of testicles, lesions of incisor teeth
Xanthine cataract	Goldmann ⁹	Perinuclear cataract and nuclear sclerosis	† Transitory hyperglycemia; disturbance in phosphorylative processes in lens and in metabolism of sulfhydryl compounds and ascorbic acid

¹This table does not include the acute, reversible opacities of the lens "cooling cataract" (Goldschmidt¹⁵), cataract associated with epinephrine shock (tum. Sudan, C., and Wyman, L. C. *Endocrinology* 27: 628, 1940), salt cataract (Goldmann and Rabinowitz¹⁶) and other forms of acute osmotic opacities of the lens in the rat (Bellows, J., and Chinn H. *Biochemistry of Lens Production of Lens Opacities by Injection of Hypertonic Solutions*, Arch. Ophth. 25: 706 [May] 1941). Demole and Knapp (*Ophthalmologica* 101: 6, 1941) have recently reported on cataracts and other ocular lesions including corneal vascularization in some rats on vitamin B₂-deficient diets.

²The allied manifestations of naphthalene cataract have been described chiefly in the rabbit.

in the blood (low calcium-phosphate ratio) and by the neuromuscular hyperexcitability, characteristic of tetany. In both forms of experimental tetany the appearance of the cortical opacities of the lens is linked closely with individual attacks of tetany rather than with some chronic dystrophic condition. This is the reason for the zonular arrangements of the opacities, frequently noted in cataract associated with experimental tetany²⁶ (fig. 10).

On the other hand, galactose and xylose cataract and cataract associated with experimental diabetes are characterized by the high monosaccharide concentration of the blood²⁷ and by the associated polyuria and polydipsia²⁸. In addition, these three types of cataract are characterized by the occurrence of a great number of vacuoles and clusters of vacuoles at the equator and in the superficial cortex of the lens at some stages of the development of the cataract. Figure 11 may serve

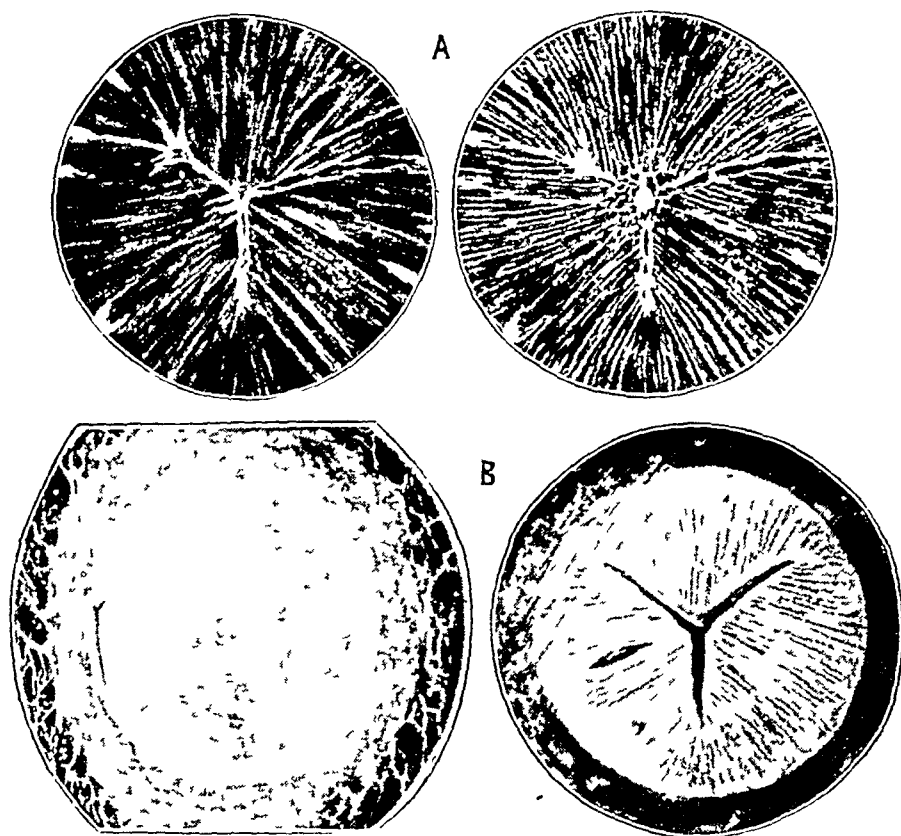


Fig. 9—Cataract produced by chronic thallium poisoning in the rat (from Donski, J. *Arch f Ophth* **128** 294, 1932). *A*, early stages, *B*, later stages.

to illustrate this. There is strongly suggestive evidence that osmotic disturbances play an important role in the pathogenesis of the diabetic group of cataracts.

Allied manifestations of naphthalene cataract have been described mainly in the rabbit, though the occurrence of this cataract has also been reported in the rat.²⁹ The observations on early naphthalene poisoning can be summarized as follows:

26 (a) Goldmann (b) von Bahr, G. *Acta ophth*, 1936, supp. 11, p. 1. (c) Siegrist, A. *Der graue Altersstar*, Berlin, Urban & Schwarzenberg, 1928.

27 (a) Darby and Day.⁹ (b) Day, P. L. *J. Nutrition* **12** 395, 1936. (c) Richter, C. P., and Schmidt, E. C. H., Jr. *Endocrinology* **28** 178, 1941.

28 (a) Sullmann and Weekers.^{4a} (b) Sasaki, T. *Arch f Ophth* **138** 351, 365 and 380, 1938. (c) Bakkei, A. *ibid* **140** 531, 1939. (d) Richter, C. P. *Am J Physiol* **133** 29, 1941.

29 Goldmann, H. *Klin Monatsbl f Augenh* **83** 433, 1929.

1 Disturbances in the early phases of carbohydrate metabolism These include transitory hyperglycemia³⁰, disturbance of phosphorylative processes in the lens,³¹ and increase in the lactic acid content of the lens, aqueous and blood³¹

2 Disturbances of the redox substances of the lens formation and excietion of mercapturic acid by the binding of sulfydryl compounds³², loss of sulfydryl compounds from the lens³¹, loss of ascorbic acid from the aqueous a few hours after poisoning,³³ and loss of reducing power of the lens against ascorbic acid³⁴

It is likely that these two groups of manifestations of naphthalene poisoning are related to each other Obviously, some of these manifestations point to a

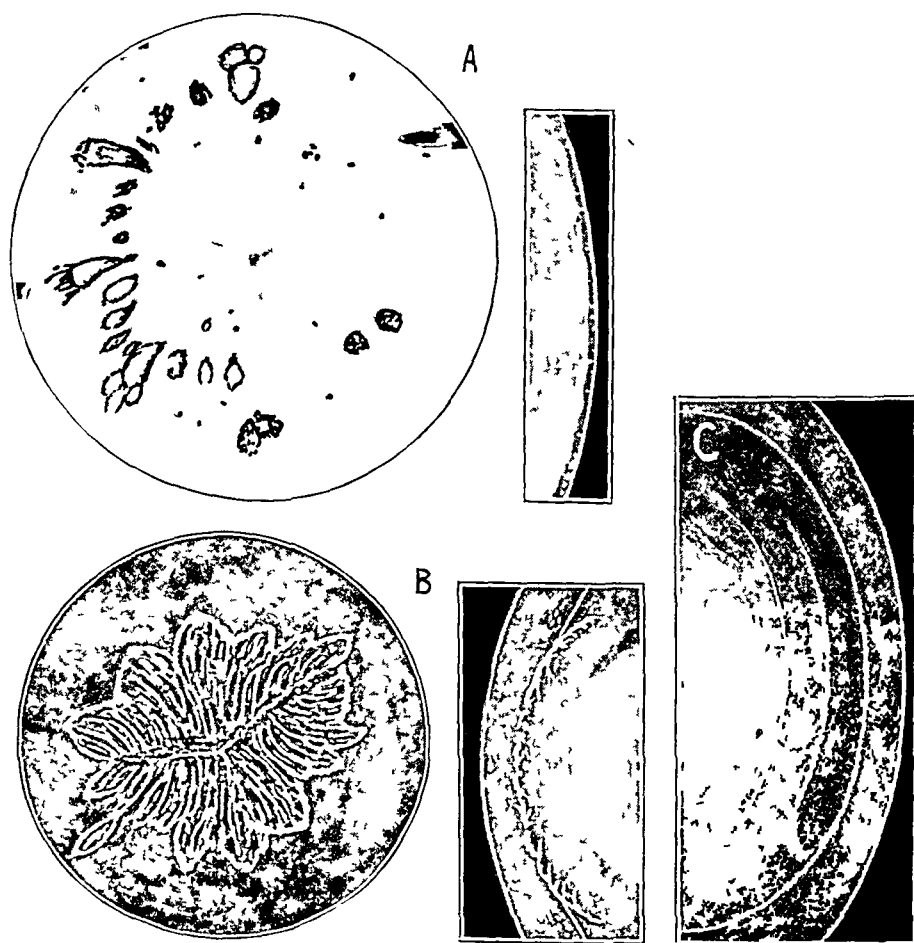


Fig 10—Cataract associated with experimental tetany in a parathyroidectomized rat (from Goldmann³) A, early stage, B and C, later stages

pathogenic relation to the diabetic group of cataract, however, the appearance with the slit lamp and the absence of conspicuous polydipsia indicate that osmotic dis-

30 Michael, D, and Vancea, P Klin Monatsbl f Augenh 78 285, 1927 Komura, K Arch f Ophth 120 766, 1928

31 Müller, H K Arch f Ophth 140 191, 1939

32 Bourne, M C, and Young, L Biochem J 28 803, 1934 Stekol, J A J Biol Chem 110 463, 1935, 121 87, 1937

33 Müller, H K, and Buschke, W Arch f Augenh 108 368, 1934

34 Müller, H K Arch f Augenh 109 304, 1935

turbances play a less important role in the production of naphthalene cataract. At present, this cataract must be left unclassified.

On the basis of the special features of the cataracts and of their allied manifestations, tryptophan deficiency cataract must be differentiated both from the diabetic and from the tetanic group of experimental cataracts in the rat. On the other hand, it can be classified with thallium cataract and with the cataract developing in the presence of riboflavin deficiency, and these cataracts may be said to constitute the dystrophic group.

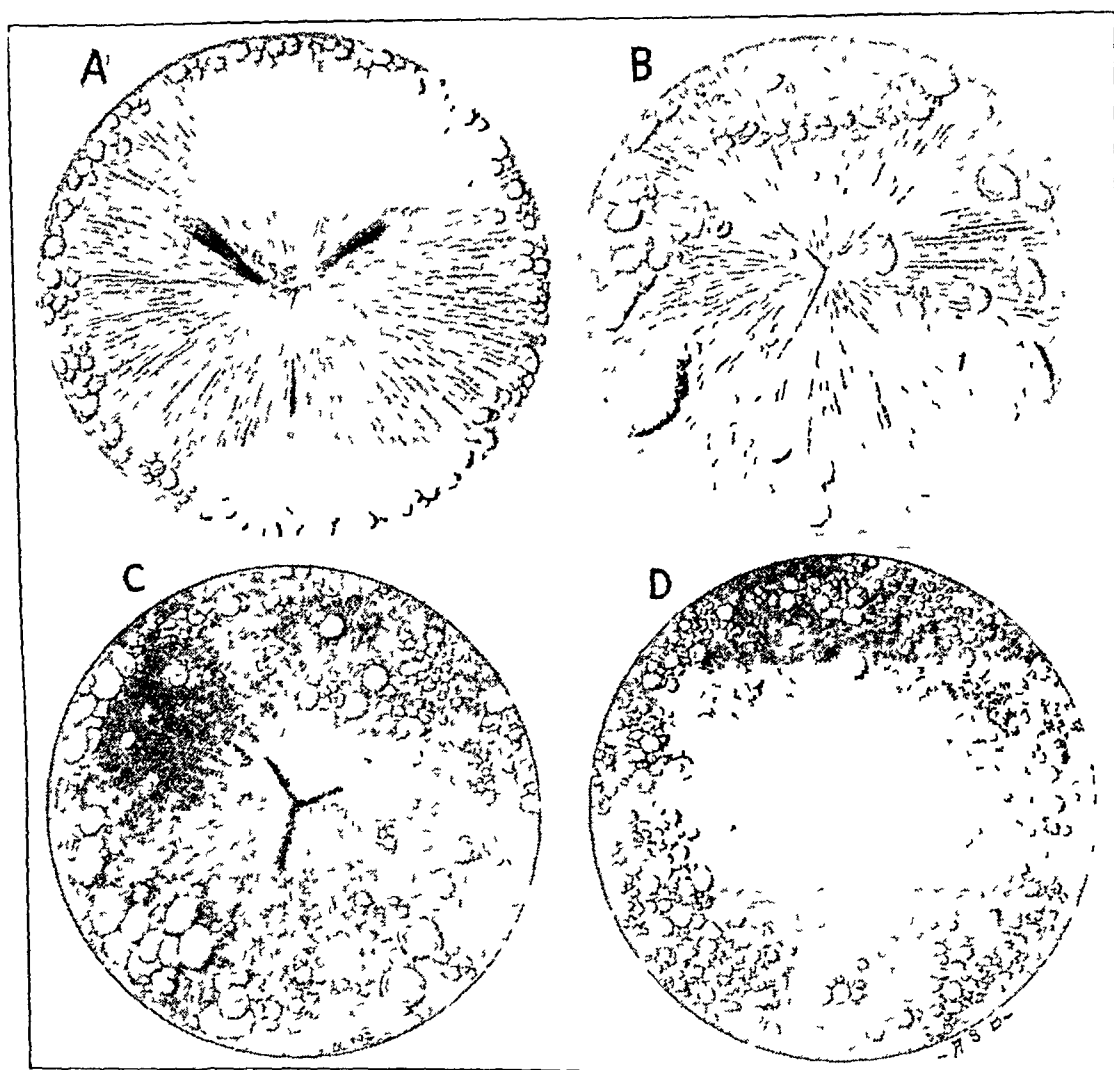


Fig 11—*A* and *B*, cataract associated with experimental diabetes in pancreatectomized rats (from Richter and Buschke, to be published). *C*, cataract produced in a 55 Gm rat fed a 50 per cent galactose diet for four days. The drawing was made eight days later. *D*, cataract produced in a 38 Gm rat fed a 50 per cent xylose diet for six days. The drawing was made five days later.

Among the symptoms of cataracts of the dystrophic group just enumerated are vascular and inflammatory reactions, which are not commonly classified as dystrophic. Similar lesions, however, are well known features of various deficiency diseases, both in men and in experimental animals. The occurrence of such symptoms, e g, keratitis, corneal vascularization and dermatitis, as part of certain syndromes which are characterized by other, more familiar, dystrophic signs should, therefore, occasion no surprise.

THE DYSTROPHIC GROUP OF CATARACTS

The similarity of the distribution of manifestations of the dystrophic group of cataracts and the embryonic relation of some of the affected structures suggest a metabolic relation both of the affected tissues and of the various syndromes

According to Bietti,³⁵ rats can be protected against cataract and other manifestations of thallium poisoning by brewers' yeast and, to a lesser degree, by liver injection N N R, by autoclaved brewers' yeast or by pure riboflavin. The strong protective effect of brewers' yeast against the cataract was found to be confined to thallium cataract, and practically no protection against the cataracts produced by naphthalene, galactose, lactose and alimentary hypocalcemia was observed.

In a subsequent report the human "metabolic" cataracts will be correlated with the classification of experimental cataracts suggested here, and the relation of human dystrophic cataracts to experimental dystrophic cataracts will be discussed.

SUMMARY

Cataract associated with tryptophan deficiency occurs in at least two forms, the acute and the chronic. Details of the morphologic character and development of the cataract are described. Arrest of the cataract associated with acute tryptophan deficiency by administration of tryptophan has been observed. No complete loss of bound indole occurs even in the advanced stages of tryptophan deficiency cataract.

Cataracts associated with tryptophan deficiency, riboflavin deficiency and thallium poisoning are similar with respect both to the presence of allied symptoms in the cornea, skin and testicles and to certain morphologic and developmental features by which they are distinguished from diabetic and tetanic cataracts.

On the basis of their morphologic character and development and of the allied symptoms, a classification of the experimental cataracts in the rat is suggested. The three principal groups in this classification are the diabetic, the tetanic and the dystrophic groups. The diabetic group includes galactose and xylose cataracts and cataract associated with experimental diabetes, the tetanic group, the cataracts occurring in the course of dietary and postoperative tetany, and the dystrophic group, the cataracts accompanying riboflavin deficiency, chronic thallium poisoning and tryptophan deficiency.

The slit lamp drawings of cataracts and corneal vascularization associated with tryptophan deficiency and of the cataracts in diabetes and those produced by galactose and xylose diets were made by Mrs. Annette S. Burgess.

³⁵ Bietti, G. *Med. sper., Arch. ital.* 73, 1941, abstracted, *Zentralbl. f. d. ges. Ophth.* 46: 502, 1941.

DYSTROPHIC CATARACTS AND THEIR RELATION TO OTHER "METABOLIC" CATARACTS

WILHELM BUSCHKE, M D

BAI TIMORE

In the various papers on cataract, generalizations concerning cataract as the result of local or general nutritional disturbances, endocrine disturbances, osmotic disturbances and others have led to much confusion. In a previous paper¹ I outlined a classification of experimental cataracts as diabetic, tetanic and dystrophic, on the basis of their allied manifestations and developmental features. The object of this paper is to correlate this classification with the "metabolic" cataracts observed in human beings and, in particular, to discuss the relation of the experimental and the clinical cataracts of the dystrophic group. The object of this classification is not primarily a diagnostic one, but is the unification and differentiation of features which should help in delimiting the various groups of cataract and the consideration of these groups from the standpoint of the difference in pathogenesis.

In the bibliographic analysis² that follows, attention has been especially focused on the dystrophic group. The diabetic and the tetanic group are presented briefly chiefly for purposes of contrast.

BIBLIOGRAPHIC ANALYSIS OF TYPES OF CATARACT

There are some forms of cataract, e. g., those associated with dimethylphenol and with ergot poisoning, which in the present state of knowledge show no relation whatever to any one of the three groups which have been differentiated in this discussion. Of the unclassified forms, only the cataract due to damage from roentgen rays is discussed, this form is described briefly to illustrate the possibility that further knowledge may establish a relation between damage produced by roentgen rays and the dystrophies.

I The Diabetic Group

- 1 True diabetic cataract in man³
- 2 Experimental diabetic cataract in dogs⁴ and rats⁵

From the Wilmer Ophthalmological Institute of the Johns Hopkins University School of Medicine

1 Buschke, W. Classification of Experimental Cataracts in the Rat. Recent Observations of Cataract Associated with Tryptophan Deficiency and with Some Other Experimental Conditions, *Arch Ophth* **30** 735 (Dec) 1943

2 No attempt is made here to give a complete bibliography of the literature on "metabolic" cataracts and on theories of cataract formation. The reader may be referred to reviews and discussions by the following authors: (a) Siegrist, A. *Der graue Altersstar*, Berlin, Urban & Schwarzenberg, 1928. (b) Bourne, M. C. *Physiol Rev* **17** 1, 1937. (c) Bellows, J. G., and Chinn, H. Theories of Cataract, *Arch Ophth* **26** 1066 (Dec) 1941. (d) Duke-Elder, W. S. *Textbook of Ophthalmology*, St. Louis, C. V. Mosby Company, 1941, vol. 3.

3 Schnyder, F. W. *Klin Monatsbl f Augenh* **70** 45, 1923. O'Brien, C. S., Molsberry, I. M., and Allen, J. H. Diabetic Cataract: Incidence and Morphology in One Hundred and Twenty-Six Young Diabetic Patients, *J A M A* **103** 892 (Sept 22) 1934.

4 Chaikoff, L., and Lachman, G. S. *Proc Soc Exper Biol & Med* **31** 237, 1933.

5 Richter, C. P., and Buschke, W. To be published.

3 Lactose and galactose cataract in rats,⁶ rabbits⁷ and mice⁷

4 Xylose cataract in rats⁸

The most conspicuous allied manifestations¹ are increased appetite, polydipsia and polyuria and a high monosaccharide concentration in the blood. A characteristic morphologic feature of the cataracts due to galactose and xylose and to experimental diabetes in the rat is the accumulation in clusters of a large number of cortical and subcapsular vacuoles, particularly at the equator of the lens, in some stages¹. It is suggestive that the subcapsular vacuoles which are seen in large numbers in some cases of human diabetic cataract, and which have been stated to be characteristic by some authors,⁹ are the equivalent of the much more massive vacuolar changes in the experimental cataract forms of this group.

The evidence points strongly to osmotic disturbances as a pathogenic factor in this entire group of cataracts. This possibility has been noted before in connection with individual members of the group.¹⁰

II The Tetanic Group

1 Cataract associated with postoperative hypoparathyroidism in man¹¹

2 Cataract associated with idiopathic tetany in man¹¹

3 Cataract associated with experimental postoperative hypoparathyroidism in dogs,¹² rats¹³ and rabbits^{13b}

4 Experimental dietary tetanic cataract in rats^{11a} and rabbits¹⁴

5 Possibly some zonular cataracts¹⁵

It is possible, but so far undecided, that the cataracts which have been observed in cases of Gee-Herter disease (Herter-Heubner disease, intestinal infantilism, celiac disease, nontropical spue) and which are accompanied by tetany belong to the tetanic group.¹⁶ The same may be said of cataract associated with osteomalacia.¹⁷

The most conspicuous allied manifestations are neuromuscular hyperexcitability and a lowered ratio of calcium to phosphate in the blood. This group of cataracts has some allied disturbances (lesions of the skin, hair, nails and teeth) in common with cataracts of the dystrophic group.

6 Mitchell, H. S., and Dodge, W. M. *J. Nutrition* **9** 37, 1935. Yudkin, A. M., and Arnold, C. H. Cataracts Produced in Albino Rats on a Ration Containing a High Proportion of Lactose or Galactose, *Arch. Ophth.* **14** 960 (Dec.) 1935.

7 Unpublished observations.

8 Darby, W. J., and Day, P. L. *Proc. Soc. Exper. Biol. & Med.* **41** 507, 1939; *J. Biol. Chem.* **133** 503, 1940.

9 (a) Meesmann, A. *Die Mikroskopie des lebenden Auges an der Gullstrandschen Spaltlampe*, Berlin, Urban & Schwarzenberg, 1927, p. 123. (b) Duke-Elder, W. S. *Recent Advances in Ophthalmology*, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1934, p. 336, footnote 2 d, p. 3206.

10 Sullmann, H., and Weekers, R. *Ztschr. f. Augenh.* **95** 58, 1938. Bakker, A. *Arch. f. Ophth.* **140** 531, 1939. Bellows and Chinn^{2c}. Duke-Elder,^{2b} p. 354. Duke-Elder,^{2d} p. 3208.

11 Reviewed by (a) von Bahr, G. *Acta ophth.*, 1936, supp. 11, p. 1. (b) Meesmann, A. *Hypocalcaemie und Linse*, Stuttgart, Ferdinand Enke, 1938. (c) Duke-Elder^{2d}.

12 Siegrist^{2a}. Duke-Elder^{2d}.

13 (a) Erdheim, J. *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **16** 632, 1906. (b) Goldmann, H. *Arch. f. Ophth.* **122** 146, 1929.

14 Swan, K. C., and Salit, P. W. *Am. J. Ophth.* **24** 611, 1941.

15 von Bahr^{11a}. Meesmann^{11b}.

16 Bennett, T. I., Hunter, D., and Vaughan, J. M. *Quart. J. Med.* **1** 603, 1932. Bangerter, A. *Ophthalmologica* **98** 291, 1940.

17 Maxwell, J. P., and Pi, H. T. *Proc. Roy. Soc. Med.* **33** 777, 1940.

A morphologic and developmental feature of the tetanic group is the zonular development of the opacities in connection with the periodic action of the damaging factor or factors in the experimental cataracts¹⁸ and probably in some clinical forms,¹¹ and the close time relation between the development of the opacities of the lens and the occurrence of the systemic changes typical of tetany.

It is of interest in this connection that cyclic changes in activity, mood and craving for calcium associated with both experimental and clinical tetany have been observed.¹⁹

III The Dystrophic Group

A Experimental conditions

- 1 Cataract associated with experimental riboflavin deficiency in rats²⁰
- 2 Cataract due to chronic thallium poisoning in rats and mice²¹
- 3 Cataract associated with experimental tryptophan deficiency in rats¹

B Clinical cataract syndromes with predominantly atrophic dermatoses

- 4 Cataracta syndematotica associated with poikiloderma vasculare atrophicans (Rothmund syndrome)²²
- 5 Cataracta syndematotica associated with scleroderma (Weiner syndrome)²³

C Clinical cataract syndromes with atopic dermatitis

- 6 Cataracta syndematotica with atopic eczema, neurodermatitis, chronic neurodermatitis (Andogsky syndrome)²⁴ and Besnier's prurigo with ichthyosis²⁵

D Clinical cataract syndromes associated with other cutaneous conditions

- 7 Cataracta syndematotica in rare cases of keratosis follicularis²⁶ (Darier's disease), telangiectasis²⁷ and myxedema²⁸
- 8 Cataract with developmental anomalies of the hair, such as curly hair and aplasia pilaris²⁹

E Other clinical cataract syndromes of the dystrophic group

- 9 Cataract associated with mongolism³⁰
- 10 Cataract associated with dystrophia myotonica³¹

18 Siegrist^{2a} Duke-Elder^{2d} Goldmann^{13b}

19 Richter, C. P., Honeyman, W. M., and Hunter, H. *J. Neurol. & Psychiat.* **3**:19, 1940

20 Reviewed by Cosgrove, R. W., and Day, P. L. *Am. J. Ophth.* **25**:544, 1942. Cataract has recently been observed also in pigs on riboflavin-deficient diets (Wintrobe, M. M., Buschke, W., Folts, R. H., Jr., and Humphreys, S. To be published)

21 Reviewed by (a) Buschke, A., and Peiser, B. *Ergebn. d. allg. Path. u. path. Anat.* **25**:1, 1931. (b) Donski, J. *Arch. f. Ophth.* **128**:294, 1932

22 Reviewed by Schnyder, F. W. *Schweiz. med. Wchnschr.* **16**:719, 1935

23 Reviewed by Siegrist^{2a} Oppenheimer, B. S., and Kugel, W. H. *Am. J. M. Sc.* **202**:629, 1941. Agatston, S. A., and Gartner, S. Precocious Cataracts and Scleroderma (Rothmund's Syndrome, Werner's Syndrome). Report of Case, *Arch. Ophth.* **24**:492 (March) 1939

24 Reviewed by Beetham, W. B. Atopic Cataracts, *Arch. Ophth.* **24**:21 (July) 1940

25 Kugelberg, I. *Klin. Monatsbl. f. Augenh.* **92**:484, 1934

26 Gjersing, O. M., cited by Franceschetti, A., in Schneck, F., and Bruckner, A. *Kurzes Handbuch der Ophthalmologie*, Berlin, Julius Springer, 1930, vol. 1, p. 754

27 Nieden, A. *Zentralbl. f. Augenh.* **11**:353, 1887. Friedenwald, J. S. Unpublished data

28 Lowenstein, A. *Klin. Monatsbl. f. Augenh.* **76**:539, 1926

29 Weiner, S. *Acta ophth.* **6**:382, 1928. Papastratigakis, C. *Paris med.* **12**:475, 1922. Cederkreutz, A. *Zentralbl. f. Haut- u. Geschlechtskr.* **21**:841, 1927

30 Reviewed by van der Scheer, W. M. *Klin. Monatsbl. f. Augenh.* **62**:155, 1919

31 Reviewed by Allen, J. H., and Barer, C. G. Cataract of Dystrophia Myotonica, *Arch. Ophth.* **24**:867 (Nov.) 1940

CATARACTS OF THE DYSTROPHIC GROUP

A brief discussion of the various cataracts of the dystrophic group follows, with some bibliographic references

A EXPERIMENTAL CONDITIONS

1 Riboflavin Deficiency—Cataract Day and associates³² observed cataract in animals fed a diet deficient in the heat-stable fraction of the vitamin B complex then called vitamin G. The incidence of this form of cataract varied from zero to almost 100 per cent in various laboratories³³. The possible role of the susceptibility of special strains has been pointed out^{33d}.

The specific relation of the cataract to riboflavin has been demonstrated by the protective and curative (arresting) effect of this substance³⁴. However, the relation of this cataract to riboflavin deficiency is not simple, while some authors have claimed that the small amount of riboflavin present in certain caseins may explain failure to produce cataract,³⁵ others have asserted that the incidence of cataract is higher if traces of riboflavin are added to diet³⁶.

It appears that a factor or factors other than riboflavin may influence the manifestation of this cataract. With this qualification, one may speak of a riboflavin deficiency cataract.

According to O'Brien,^{3-b} the development of the cataract does not follow any rule. Nuclear, cortical and anterior and posterior subcapsular opacities were observed in various combinations in different animals, and even in the two eyes of the same animal.

Other manifestations. Signs of riboflavin deficiency in the organs are (1) arrest of body growth³⁷, (2) dermatosis with alopecia³⁸, (3) keratitis²⁰, (4) lesions of the testicles³⁹, (5) nerve lesions,³⁹ and (6) lesions in the endocrine organs, such as the thymus³⁹.

2 Experimental Chronic Thallium Poisoning—Cataract. Cataract in rats and mice with chronic thallium poisoning was observed by A. Buschke.⁴⁰

The cataract begins with anterior subcapsular changes. The cortex becomes progressively opaque, suddenly perinuclear and fine nuclear clouding occurs^{21b}.

Thallium cataract did not develop in older rats. Some investigators were not able to produce mature thallium cataract,⁴¹ and still others observed great individual

32 (a) Day, P. L., Langston, W. C., and O'Brien, C. S. *Am J Ophth* **14** 1005, 1931.
(b) O'Brien, C. S. *Experimental Cataract in Vitamin G Deficiency*, *Arch. Ophth* **8** 880 (Dec.) 1932. (c) Day, P. L. *J Nutrition* **12** 395, 1936. (d) Day, P. L., and Langston, W. C. *ibid* **7** 97, 1934.

33 (a) Cosgrove and Day²⁰ (b) Gyorgy, P. *Biochem J* **29** 741, 1935. (c) Bourne, M. C., and Pyke, M. A. *ibid* **29** 1865, 1935. (d) Bessey, O. A., and Wolbach, S. B. *J Exper Med* **69** 1, 1939. (e) Richardson, L. R., and Hogan, A. C., cited by Bessey and Wolbach. (f) Eckardt, R. E., and Johnson, L. V. *Nutritional Cataract and Relation of Galactose to Appearance of Senile Suture Line in Rats*, *Arch Ophth* **21** 315 (Feb.) 1939. (g) Footnote 32.

34 Day, P. L., Darby, W. J., and Cosgrove, K. W. *J Nutrition* **15** 83, 1938.

35 Day, P. L., and Darby, W. J. *Biochem J* **32** 1171, 1938.

36 Baum, H. M., Michaelree, J. F., and Brown, E. B. *Science* **95** 24, 1942.

37 Kuhn, R., Rudt, H., and Wagner-von Jauregg, T. *Ber d deutsch chem Gesellsch* **66** 1950, 1933.

38 Sullivan, M., and Nicholls, J. *J Invest Dermat* **4** 181, 1941.

39 Shaw, J. H., and Phillips, P. H. *J Nutrition* **22** 345, 1941.

40 Buschke, A. *Arch f Dermat. u Syph* **116** 477, 1913.

41 von Mellin, A. *Experimentelle Untersuchungen über die Entstehung des Thallium-Stares nebst Bemerkungen über eine neue vererbare und angeborene Starform bei weissen Ratten*, Munich, K. Albersstoecker, 1926.

differences in the development of the cataract and familial variation in susceptibility⁴², in particular, the rapidity with which the opacities developed was subject to familial variation

Other Manifestations Changes in other organs are (1) arrest of body growth^{21a}, (2) alopecia^{21a}, (3) keratitis and corneal vascularization^{42a}, (4) iritis^{42a}, (5) testicular lesions^{21a}, (6) lesions in other endocrine organs,^{21a} including the adrenals, the thyroid, the pancreas, the islets of Langerhans and the parathyroids, (7) nerve lesions^{21a}, (8) rachitic changes in bone,^{21a} and (9) inflammatory and metaplastic changes in the gastrointestinal tract^{21a}

3 Experimental Tryptophan Deficiency—Cataract⁴³ The morphologic features and development of this cataract have been described in a previous report¹ An acute and a chronic type of cataract have been observed The acute type involves first the cortex and later the perinuclear and nuclear zones The chronic type is confined to the cortex

Allied Manifestations Changes in other organs are (1) arrest of body growth⁴⁴, (2) corneal vascularization and keratitis⁴³, (3) cutaneous lesions and alopecia,⁴⁴ and (4) testicular atrophy and aspermatogenesis⁴⁵ Lesions in the incisor teeth have been observed, too, in animals on a tryptophan-deficient diet⁴⁶, the relation of these lesions to tryptophan deficiency demands further study

The occurrence of a hypochromic anemia in animals on tryptophan-deficient diets has been reported^{46a}

Histopathologic studies which are being carried on by Dr L Emmett Holt Jr and his associates may reveal other pathologic manifestations of tryptophan deficiency, in addition to those mentioned here

B CLINICAL CATARACT SYNDROMES WITH PREDOMINANTLY ATROPHIC DERMATOSES

4 Rothmund Syndrome⁴⁷—Cataract The cataract develops rapidly in early childhood (between the second and the sixth year of age) and becomes mature within a few days to months It begins in the anterior and the posterior cortex (Siegrist^{2a}) Later the nucleus becomes milky, and a dense perinuclear, shell-like opacity is formed

Other Manifestations Changes in other organs are (1) dermatosis poikiloderma vasculare atrophicum (Jacobi) and (3) atrophy and underdevelopment of the gonads in both sexes²²

The disease is probably inherited as a recessive⁴⁸

5 Werner Syndrome⁴⁹—Cataract The cataract develops in the third or fourth decade of life Opacities of various sizes are seen in the posterior and the anterior

42 (a) Ginsberg, S, and Buschke, A Klin Monatsbl f Augenh **71** 385, 1923 (b) Mamoli, L Ann di ottal e clin ocul **55** 35, 1927

43 (a) Totter, J R, and Day, P L J Biol Chem **140** cxxxiv, 1941, (b) J Nutrition **24** 159, 1942 (c) Buschke, W, Albanese, A A, and Follis, R H, Jr Federation Proc **1** 175, 1942 (d) Albanese, A A, and Buschke, W Science **95** 584, 1942

44 Berg, C P, Rose, W C, and Marvel, C S J Biol Chem **85** 207 and 219, 1929

45 Shettles, L B Proc Ann Conf Biol Spermatozoa, 1942, p 28

46 Buschke and associates^{43c}

46a Albanese, A A, Randall, R McI, and Holt, L E, Jr Science **97** 312, 1943

47 Rothmund, A Arch f Ophth (pt 1) **14** 159, 1868 Seefelder, R Ztschr f Augenh **86** 81, 1935

48 Vogt, A Lehrbuch und Atlas d Spaltlampenmikroskopie des lebenden Auges, Berlin, Julius Springer, 1931, vol 2

49 Werner, C W O Ueber Katarakt in Verbindung mit Sklerodermie, Inaug Dissert, Kiel, Schmidt & Klaunig, 1904

cortex, larger opacities, in the form of "bread crumbs," are seen at the posterior pole (Kugelberg²⁵) Nuclear cataract has been described, in addition to cortical opacities⁵⁰

Occurrence of the disease in siblings and in several generations of the same family has been reported⁵¹

Other Manifestations Changes in other organs are 1 Dermatosclerosis⁵², changes in the hair, such as premature graying and baldness,⁵² and ulcers⁵¹ 2 Atrophy of the testicles and aspermatogenesis, premature sexual involution in the female⁵² 3 Endocrine manifestations⁵¹ hyperparathyroidism, adenomas of thyroid and adrenal cortex, abnormal blood sugar curve 4 Keratitis bullosa⁵³

Marchionini and Lux⁵⁴ described a case of scleropoikiloderma (Arndt-Jaffe) with anterior and posterior cortical and subcapsular cataract in a patient aged 30 Clinically and histologically the skin exhibited features of scleroderma and poikiloderma, and changes in the endocrine glands similar to those associated with scleroderma were noted

Possibly the few instances of cataract in cases of telangiectasis of the skin of the face, hands and arms (Nieden, Friedenwald²⁷) also belong in this group

C CATARACT SYNDROMES WITH DERMATOSES OF THE ATOPIC DERMATITIS TYPE

6 *Andogsky Syndrome*⁵⁵—Cataract Two types of cataract have been described (Beetham^{56a}) The one starts at the posterior pole, spreading later to the anterior cortex and the nucleus, the other begins as an anterior subcapsular rosette, in which a dense, umbrella-shaped opacity with concave margins develops Later the anterior and the posterior cortex become opaque, and the cataract matures within several months or years It occurs in the second or third decade of life

Other Manifestations Changes in other organs are 1 Superficial keratitis⁵⁷ (keratitis epithelialis vesiculosa disseminata, keratitis superficialis punctata) It appears concomitantly with the attacks of eczema Subjective symptoms may be insignificant, and the corneal changes may escape notice without the use of the slit lamp 2 Dermatosclerosis⁵⁸ atopic dermatitis (synonyms atopic eczema, lichen chronicus [Vidal], *prunigo diathésique* [Besnier], *neurodermite diffuse* [Brocq-Jacquet] atopy [Coca], allergic eczema on a constitutional basis [Juelg])

No unequivocal evidence for the presence of endocrine disorders could be found in the literature, although claims to that effect have been made⁵⁸

3 Manifestations of hypersensitiveness, either in the patients themselves or in their family—(asthma, hay fever, eosinophilia, multiple cutaneous reactions)⁵⁹

50 Vossius, A Ztschr f Augenh **43** 640, 1920

51 (a) Footnote 23 (b) Mamou, H Sclerodermie et cataracte, Thesis, Paris, 1931 (c) Krebs E Hartmann, E, and Thiebaut, F Rev neurol **53** 606, 1930

52 Werner⁴⁹ Footnote 51

53 Kleiber Klin Monatsbl f Augenh **65** 923, 1920

54 Marchionini, A, and Lux, L Arch f Dermat u Syph **176** 309, 1937

55 Andogsky, N Klin Monatsbl f Augenh **52** 842, 1914

56 (a) Beetham²⁴ (b) Kugelberg²⁵ (c) Vogt, A Schweiz med Wchnschr **51** 669, 1921 (d) Vogt,⁴⁸ p 557

57 Vogt,⁴⁸ 1930, vol 1 p 170 Pillat, A Wien klin Wchnschr **50** 768 1937

58 (a) Coca A F Specific Diagnosis and Treatment of Allergic Diseases of Skin, J A M A **103** 1275 (Oct 27) 1934 (b) Footnote 56

59 Beetham²⁴ Kugelberg²⁵

No evidence for an allergic origin of the cataract could so far be adduced⁶⁰ There now exists general agreement as to the familial character of the atopic dermatitis⁶¹

Kugelberg²⁵ described cataract in association with ichthyosis vulgaris, Besnier's prurigo, hypogenitalism and developmental lesions of the teeth The cataract appeared in the form of irregularly disseminated fine opacities, both in the anterior and in the posterior cortex, predominantly subcapsular The cutaneous lesions occurred in several members of the family Whether the combination of manifestations described by Kugelberg is due to coincidence or to a combination of two hereditary syndromes may be left open to question

D CLINICAL CATARACT SYNDROMES ASSOCIATED WITH OTHER CUTANEOUS CONDITIONS

7 *Cataract Associated with Keratosis Follicularis (Daniel's Disease*²⁶), *Telangiectasis*²⁷ and *Myxedema*⁶²—The association of cataract with myxedema is commonly referred to in papers on metabolic or dystrophic cataract I found only 5 cases in the literature In 3 of these 5 cases other causes (tetany, senile cataract) were not ruled out In view of the relative frequency of myxedema and cretinism, one would expect a more frequent occurrence of cataract in either of these conditions if thyroid insufficiency were a primary factor in the development of cataract

8 *Cataract Associated with Anomalies of the Hair*²⁹—A few scattered observations have been made on the association of anomalies of the hair (curly hair, alopecia, and aplasia pilaris) with juvenile cataract

E OTHER CLINICAL CATARACT SYNDROMES OF THE DYSTROPHIC GROUP

9 *Cataract Associated with Mongolism*⁶³—The most frequent form of cataract associated with mongolism³⁰ is the "cataracta punctata disseminata," or "snowflake cataract" A great number of dotlike or flakelike opacities appear either throughout all the layers or only in the cortex In addition, a star of intensely white opacities appears near the anterior or the posterior pole of the lens In a series of 60 patients with mongolism, van der Scheer³⁰ found cataract in none under 8 years of age, in 61 per cent of the patients from 8 to 17 years of age and in 100 per cent of the patients beyond 17 years of age This indicates that persons with mongolism are liable to have cataract if they live long enough, i e, beyond the age of 17 years However, such persons die at an average age of 14 years, and 40.5 per cent die

60 Brunsting, L. A. Atopic Dermatitis (Disseminated Neurodermatitis) of Young Adults. Analysis of Precipitating Factors in One Hundred and One Cases and Report of Ten Cases with Associated Juvenile Cataract, *Arch Dermat & Syph* **34** 935 (Dec.) 1936
Daniel, R. K. Allergy and Cataracts, *Tr Sect Ophth, A. M. A.*, 1935, p. 50
Woods, A. C., in discussion on Daniel, p. 55
Beetham²⁴

61 (a) In order to avoid misunderstandings, I refer here to the classification of dermatoses associated with hypersensitivity by Coca and Sulzberger^{58a} (1) atopic dermatoses, of familial occurrence, (2) contact dermatitis, nonfamilial, and (3) fungous dermatitis, or eczematous dermatophytosis It is to be understood that the cataract syndrome under discussion has to do with the first of these three conditions (b) Holt, L. E., Jr., and McIntosh, R. *Diseases of Infancy and Childhood*, ed. 11, New York, D. Appleton-Century Company, Inc., 1939

62 (a) Lowenstein²⁸ (b) Callen, P. A. *Tr Am Ophth Soc* **7** 391, 1895 (c) Dutoit, A. *Ztschr f Augenh* **32** 139, 1914 (d) Cantonnet, M. A. *Ann d'ocul* **143** 475, 1920 (e) Nitzulescu, J. *Zentralbl f d ges Ophth* **15** 847, 1926

63 Pearce, F. H., Rankin, R., and Ormond, A. W. *Brit M J* **2** 186, 1910
Ormond, A. W. *Tr Ophth Soc U Kingdom* **32** 69, 1911

even before the age of 5 years⁶⁴ The more extensive opacities are usually observed in patients beyond the age of 12 years

Other Manifestations⁶⁴ Changes involving other organs are (1) mongoloid habitus, such as peculiarities of lid fissures and epicanthus, (2) idiocy, (3) skeletal changes, (4) developmental anomalies of the teeth and retardation and irregularities of the first and the second dentition, (5) various anomalies of the skin, trophic disturbances of the nails and sparse hair and a tendency to eczema, (6) atrophy of the testicles and cryptorchism, sexual infantilism in both sexes and sterility, (7)

Synoptic Table of

Condition	Special Features of Cataract with Regard to Occurrence and Morphologic Character	Allied			
		Cornea	Skin and Adnexa	Gonads	Teeth
Experimental riboflavin deficiency	Cortical and nuclear, outspoken variability in occurrence and morphologic character, occurs only in young rats	Vascularization, keratitis	Dermatitis and alopecia	Atrophy of testicles, aspermatogenesis, anestrus	
Experimental thallium poisoning	Cataract begins in cortex, outspoken variability in occurrence, occurs only in young rats	Vascularization	Alopecia	Aspermatogenesis, anestrus	
Experimental tryptophan deficiency	Cataract begins in cortex outspoken variability in morphologic character and development, occurs only in young rats	Vascularization, keratitis	Alopecia and other cutaneous lesions	Atrophy of testicles, aspermatogenesis	Lesions in incisor teeth *
Rothmund syndrome	Cataract begins in anterior and posterior cortex, develops in a few months, occurs in early childhood		Poikiloderma vasculare atrophicans (Jacobi), atrophic nails and hair	Atrophy of testicles, aplasia of ovaries	
Werner syndrome	Cataract begins in anterior and posterior cortex occurs in adult life (3d to 4th decade)	Bullous keratitis	Scleroderma, cutaneous ulcers, premature graying of hair, baldness	Atrophy of testicles	
Andogsky syndrome	Type 1 begins at posterior pole type 2 begins as a stellate opacity in anterior cortex develops within several months occurs in adolescent or adult life	Keratitis superficialis epithelialis punctata	Atopic dermatitis		†
Dystrophia myotonica (Batten Gibb Steinert)	Cataract begins in posterior and anterior superficial cortex many iridescent and white dots occurs from 3d decade on	Bullous keratitis	Premature baldness	Atrophy of testicles, loss of libido in both sexes	
Mongolism	Cortical and nuclear, occurs as star shaped polar opacities and "snowflake" cataract (cataracta punctata disseminata) in general appears after age of 8 years		Sparse hair, trophic anomalies of nails, tendency to eczema	Sexual under development, cryptorchism, testicular atrophy	Late and irregular dentitions

* The relation of these lesions to tryptophan deficiency demands further study

† Developmental lesions of the teeth have been described occasionally, but the question of coincidence cannot yet be answered with certainty

developmental lesions of the heart, (8) hypoplastic changes in the thyroid, and (9) various developmental anomalies

Occasional manifestations of endocrine disturbance in cases of mongolism cannot be of etiologic importance, as Fanconi⁶⁵ pointed out However, evidence points strongly either to a disturbance in the plasma of the ovum (Rosanoff⁶⁶) or to a chromosomal mutation⁶⁵

64 Brousseau K, and Bramer, H G Mongolism A Study of the Physical and Mental Characteristics of Mongolian Imbeciles, Baltimore, Williams & Wilkins Company, 1928

65 Fanconi, G Schweiz med Wchnschr 69 995 1939

66 Rosanoff, A J Manual of Psychiatry and Mental Hygiene, New York, John Wiley & Sons, Inc, 1938, chap 9

10 *Cataract Associated with Dystrophia Myotonica (Myotoma Atrophica) (Steiner-Batten-Gibb)* ⁶⁷—Cataract Cataract in this disease was first observed by Greenfield ⁶⁸ The cataract of myotonia becomes manifest at any time after the third decade of life Often senile and presenile cataract is present in the ancestors The cataract develops at a progressively earlier age in successive generations (anticipation) It begins usually as a rosette-like opacity in the posterior cortex ⁴⁸ Then innumerable dustlike, white and iridescent opacities appear both in the anterior and in the posterior cortex, leaving free the directly subcapsular zone

Dystrophic Cataracts

Manifestations					Other Manifestations (Growth, Allergy)	Intrinsic, or Genotypical Character
Bones	Neuromuscular System	Central Nervous System	Hematopoietic System	Endocrine Organs	Arrest of body growth	
	Degenerative lesions in peripheral nerves			Histologic changes in thymus		
Ricket-like lesions			Various changes in blood picture	Histologic changes in thyroids, parathyroids, adrenals, islets of Langerhans and thymus	Iritis, arrest of body growth, metaplastic changes in prestomach	
			Anemia		Arrest of body growth	
						Hereditary (recessive)
				Hyperparathyroidism, irregularities in regulation of blood sugar		Probably hereditary, occurs in siblings (possibly recessive)
					Allergic manifestations (asthma, hay fever)	Outspoken familial occurrence, occurs in siblings and in several generations
	Myotonic reaction myotonia atrophica	Changes of emotional character		Changes in thyroid, inconstant		Hereditary (dominant)
Various skeletal anomalies		Idiocy		Occasionally hypoplastic changes in thyroid	Mongoloid habitus, various developmental anomalies (heart and other organs)	Occurs in both of identical twins, but in only one of fraternal twins †

† While this does not necessarily indicate a hereditary origin, it is strong evidence of the intrinsic character of the syndrome, it is compatible with the assumption of idiopathic damage to the ovum (Rosanoff ⁶⁹) or of a chromosomal mutation (Fanconi ⁶⁵)

Other Manifestations ⁶⁹ Changes in other organs are (1) testicular atrophy and loss of libido in both sexes ⁷⁰, (2) premature baldness ⁷¹, (3) lesions of endocrine organs, such as the thyroid ⁷¹, (4) myotonic atrophy with characteristic

⁶⁷ Steiner, H. Deutsche Ztschr. f. Nervenhe. **37** 58, 1909. Batten, F. R., and Gibb, H. P. Brain **32** 187, 1909.

⁶⁸ Greenfield, J. G. Rev. Neurol. & Psychiat. **9** 169, 1911.

⁶⁹ Adie, W. J., and Greenfield, J. G. Brain **46** 73, 1923.

⁷⁰ (a) Fleischer, B. Arch. f. Ophth. **96** 91, 1918. (b) Hauptmann, A. Klin. Monatsbl. f. Augenhe. **60** 576, 1918. (c) Adie and Greenfield ⁶⁹.

⁷¹ Fleischer ^{70a}. Hauptmann ^{70b}.

myotonic reaction, most frequent in the muscles of the thumb and in the interosseous muscles of the hand,⁷² and (5) bullous keratitis⁷³

According to Vogt,⁴⁸ the muscular manifestations are not *conditio sine qua non* for the syndrome, and the changes in the lens seem to be much more frequent than the muscular alterations. In the same pedigree, cases of cataract can be found with and without muscular changes.

In spite of the presence of endocrine disturbances, no conclusive evidence exists that endocrine disturbances are the cause of the other manifestations. But it has been proved beyond doubt that the condition is hereditary.⁷⁴

UNCLASSIFIED CATARACTS

Of the many forms of cataract which in the present state of knowledge do not appear to fit clearly into any one of the three groups previously outlined, only one is described here.

Cataract Due to Damage from Roentgen Rays—This cataract begins at the posterior pole as a disklike, subcapsular, foamy opacity, which is prominent on its anterior surface. Fine subcapsular opacities appear also in the anterior cortex. The posterior opacity may expand over the whole posterior subcapsular zone, thus forming a shell. The cataract progresses slowly.⁷⁵

The first visible evidence of damage to the lens due to roentgen radiation is the formation of new, abnormal suture lines as a consequence of the arrest of growth (extension in length in this case) of the affected lens fibers.⁷⁶

The other manifestations are evident from the order of decreasing radiosensitivity of the different tissues of the body (Desjardins⁷⁷). After the lymphoid cells and polymorphonuclear leukocytes, epithelial cells, particularly the basal epithelium of the testes, the follicular epithelium of the ovary and the basal epithelium of the skin and mucous membranes, are among the most radiosensitive tissues. The corneal changes (keratitis, epithelial changes, interstitial keratitis, and vascularization of the cornea) due to damage from roentgen radiation have been reviewed by Rohrschneider and others.⁷⁸

A synopsis of the more important cataract syndromes of the dystrophic group is presented in the accompanying table.

COMMENT

Knowledge of the pathogenesis of the dystrophic cataracts is more incomplete than that of any of the other groups of "metabolic" cataracts—the diabetic and the tetanic.

Role of Endocrine Glands in "Metabolic" Cataracts—The primary importance of endocrine glands in the pathogenesis of human diabetic and of some tetanic cataracts is obvious. Lesions of the endocrine glands are often encountered also

72 Vogt⁴⁸ Footnote 70

73 Birnbacher, T. *Ztschr f Augenh* **62** 44, 1927. Maillard. *Klin Monatsbl f Augenh* **77** 217, 1926.

74 Frev, H. C. *Arch f Rassen- u Gesellsch-Biol* **17** 1, 1925. Waardenburg, P. I. *Das menschliche Auge und seine Erbanlagen*, Haag, Martinus Nijhoff, 1932.

75 Rohrschneider, W. *Klin Monatsbl f Augenh* **81** 254, 1928. Meesmann, A. *ibid* **81** 259, 1928.

76 Goldmann, H., and Liechti, A. *Arch f Ophth* **138** 722, 1938.

77 Desjardins, A. U., cited by Scott, C. M. *Some Quantitative Aspects of the Biological Action of X and γ Rays*, Medical Research Council, Special Report Series, no 223, London, His Majesty's Stationery Office, 1937.

78 Birch-Hirschfeld, A. *Klin Monatsbl f Augenh* **46** 129, 1908. Rohrschneider, W. *Arch f Ophth* **121** 537, 1929.

in cases of syndromes of the dystrophic group (table, column 11), and have been said to be responsible for the cataracts. However, the cataracts and the other manifestations of the dystrophic syndromes cannot be arrested or remedied by administration of any known endocrine glandular extract. Furthermore, cataract thus far has not been produced experimentally by the complete removal of any endocrine gland other than the pancreas or the parathyroids. An explanation of the syndromes of dystrophic cataract on a primarily endocrine basis is, therefore, not supported by clinical or experimental evidence—in contrast to the diabetic and tetanic (hypoparathyroid) cataracts.

An alternative explanation, based on the comparison of the clinical and the experimental dystrophic syndromes, will be attempted in the following section.

Distribution of Manifestations of Experimental and Clinical Dystrophies with Cataract—The most important unifying feature in the group of dystrophic cataracts is the association of these cataracts with lesions in the cornea, skin and testes (table, columns 3, 4 and 5). In contrast, the dystrophies that involve chiefly the central nervous system and those that involve chiefly the hemopoietic system are not generally complicated by cataract.

The similarity of the distribution of manifestations in the syndromes of the dystrophic group suggests a metabolic relation both of the affected tissues and of the different syndromes. It may be suggested, for example, that the affected tissues resemble one another in some aspect of their metabolism and that this common metabolic process is interrupted at various related points in the different syndromes. For this reason, it is of interest that a complex of manifestations similar to that of the clinical dystrophic syndromes can be produced experimentally by diets deficient in certain chemically known vitamins or vitamin-like substances.

Role of Heredity and Environment in the Dystrophies with Cataract—There is evidence that in all the clinical forms of dystrophic cataract an intrinsic or genotypical factor conditions the development of the lesion (table, last column).

At first sight, the attempt to group these idiopathic, endogenous conditions with those exogenous conditions produced experimentally may seem forced. Such a conception, however, is not new and is well illustrated, for example, in the analysis of the intrinsic and extrinsic factors in pernicious anemia and in the relation between pernicious anemia and tropical sprue⁷⁹. Another example is the relation between exogenous and endogenous rickets (Eliot and Park⁸⁰).

It is today a generally accepted biochemical concept that enzymatic (particularly oxidative) processes in the tissue require two main units—enzymes and coenzymes, the former being proteins, and thus likely to show genotypical (hereditary) characters,⁸¹ while the latter are vitamins or vitamin-like compounds, which are not, or are not entirely, proteins. That the same group of tissues may be affected either by the absence in food of an exogenous (extrinsic) factor or by a genotypical defect of the endogenous (intrinsic) part of the same metabolic system does not appear surprising and is compatible with modern biochemical concepts.

At present the possibility can only be suggested that some metabolic link exists between the endogenous and the exogenous forms of dystrophic cataract. In the present paper the similarity in the clinical patterns of certain exogenous and certain endogenous cataract syndromes has been pointed out. It is to be hoped that this may serve, at least partially, to delimit the field in which such metabolic links may

79 Strauss, M. B., and Castle, W. B. *New England J. Med.* **207** 55, 1932.

80 Eliot, M. W., and Park, E. A. Rickets, in Brennemann, J. *Practice of Pediatrics*, Hagerstown, Md., W. F. Prior Company, Inc., 1940, vol. 1.

81 Wright, S. *Physiol. Rev.* **41** 487, 1941.

be sought. Still other exogenous dystrophic syndromes with cataract which may be discovered in the future may have to be considered similarly in relation to the endogenous syndromes.

In this concept, emphasis is placed on the hereditary basis of primary metabolic disturbances in the tissues of the affected organs in the endogenous dystrophic syndromes. It appears that such a concept is in better agreement with the clinical and experimental observations in cases of dystrophic cataract syndromes than a theory which locates the primary disturbance only in one or several special endocrine glands.

SUMMARY

On the basis of a previously suggested classification of experimental cataracts in the rat and of a bibliographic review of experimental and clinical "metabolic" cataract syndromes, three groups of cataracts are differentiated: the diabetic (hyperglycemic), the tetanic and the dystrophic. Morphologic and developmental features of the cataracts, as well as the allied symptoms, served as criteria for this differentiation.

The similarity in the clinical pattern between the clinical members of the dystrophic group and certain exogenous experimental dystrophic conditions is pointed out. The possible significance of this similarity for the metabolic interpretation of the genotypical dystrophic syndromes with cataract is discussed.

The assumption of primary metabolic disturbances in the affected tissues on a hereditary basis accounts better for the known observations than does the theory of a primary endocrine basis of the dystrophic syndromes.

THE FITTING OF CONTACT LENSES

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AND

AMERICO ORIANI

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The fitting of contact lenses has been more or less a trial and error procedure. There is no doubt that the molded plastic lens is easier to adjust than the old type glass lens. The difficulty has been in knowing what adjustments are necessary in order to fit the individual eye. After observing thousands of contact lenses, we have worked out a scientific method of adapting these devices which has proved to be most satisfactory. Simple rules have been formulated which may be applied in every case. They eliminate guesswork and give complete assurance and confidence that the lenses will be fitted correctly and skilfully, according to plan.

PROCEDURE

In the fitting of contact lenses one must bear in mind the following factors: (1) convergence of the eyes, (2) pressure of the lids, and (3) gravity dip.

To compensate for these factors, a contact lens should be fitted so that the corneal portion will be turned slightly nasally and decentered upward.

A perfectly fitting lens is one that rests evenly on the sclera without impeding the blood vessels. No tight areas, or areas of blanching, should appear in any of the possible movements of the eye. On the other hand, there should be no loose areas beyond the corneal section.

The fitter should adhere to a definite routine in adapting the contact lens to the patient's eye. The following cardinal steps are to be observed in fitting the semi-finished lens: 1. The lens is checked for over-all size. 2. The lens is checked for rotation. 3. The fluorescein test is applied to detect (a) loose and (b) tight areas. 4. The corneal center of the lens is marked. 5. A working diagram is made.

STEP 1—Sometimes a contact lens is so large that it cannot be inserted. The size is reduced from the upper portion of the nasal margin downward and along the lower border to the temporal edge. The upper scleral portion is not disturbed unless it is absolutely necessary.

Before the lens is inserted, a horizontal line is drawn from the outer to the inner canthus of the lens with a red china-marking pencil, Blaisdell 165 T. The lens is inserted with a clear solution. If it is impossible to see the nasal and lower edges of the lens while the eye is looking temporally and upward respectively, the lens is probably too large. The lower portion of the lens for the right eye is trimmed from 2 to 9 o'clock, and the lower part of the lens for the left eye, from 10 to 3 o'clock. The lens must clear the semilunar membrane and the caruncle.

Likewise, if the temporal edge of the lens interferes with the motion of the eye by striking against the outer fornix, the lens is too large. The exact area of interference is marked, and the edge is trimmed so that the lens moves in unison with the eye.

STEP 2—Any rotation of the lens is easily observed, as the horizontal line on the lens will not remain stationary. The fitter's first consideration is to stop the

rotation by relieving excessively tight areas or by tightening loose edges. Before these areas are marked on the lens, it is made certain that the lens is in the proper position. If necessary, the lens is turned with the suction cup or the finger and is held in place. Then the exact areas which need adjustment are marked. Adjustments are repeated until the lens maintains a fixed and correct position in the eye.

STEP 3—Two drops of a 1 per cent solution of fluorescein sodium is placed in the contact lens, and the lens is filled with solution and inserted. A cobalt blue or an ultraviolet ray filter is employed in observation of the lens. The fluorescein glows with a brilliant yellow-green reflex wherever the corneal section of the lens does not touch the cornea. Where the lens is in contact with the cornea a black area will be seen. All loose areas, which are indicated by the pools of fluorescein, and all tight areas, which are evident as blanched spaces, are marked on the lens. To observe tight areas it is necessary to use a white light.

The blanching is caused by the stoppage of blood flow in the vessels. It is vitally important that only areas needing adjustment be marked. The markings should not be extended beyond the limits of the exact area requiring correction.

STEP 4—While the lens is in the eye, a mark is placed on the corneal portion directly in front of the center of the pupil. By marking the pupillary center of the eye one can determine its relation to the optical center of the lens.

STEP 5—We suggest that the following procedure be adopted as a routine. A blue point-like record of the corrective markings is made on a diagram. This is an indispensable aid to the fitter and not only serves as a permanent record but can be used as a basis for analysis and for planning the necessary adjustments.

The actual visualization of the lens on paper will be of great aid to the fitter in determining the course of action. Further, a clearly defined picture of the patient's lens can be used as a valuable means of comparison by any fitter making future adjustments.

Before elimination of either tight or loose areas, the lens should be divided into four quadrants. This procedure will enable the fitter to plan his corrections and to apply the suitable method of procedure, as outlined in the rules and diagrams in the subsequent sections of the paper.

It will be noted that these rules call for relief of either the temporal or the nasal side first, as the case may be. This means that the entire temporal or the entire nasal half of the lens, as divided by the vertical line, must be adjusted. In other instances, it will be noted that correction is called for in either the upper or the lower portion. Again, this indicates that the entire portion of the lens above or below the horizontal line must be adjusted.

In the ideally fitting lens, the pool of fluorescein is sharply defined, and there is no infiltration into the scleral portion, as indicated by the absence of loose areas. There are no pressure, or tight, areas on the sclera, as evidenced by the absence of blanched patches. However, it is not always essential to achieve this ideal result.

CORRECTION OF TIGHT, OR PRESSURE, AREAS

For relief of areas of pressure the inner scleral surface of the involved area is ground with a grit-impregnated rubber point. The rubber point is fitted on a dental mandril, inserted in the hand piece of a dental lathe. A light rotary motion is used. Pressure is not exerted, but the tool is allowed to do the grinding. All ground areas are repolished with a felt disk and a polishing compound before the lens is reinserted. All tight areas are to be eliminated before the loose areas are adjusted.

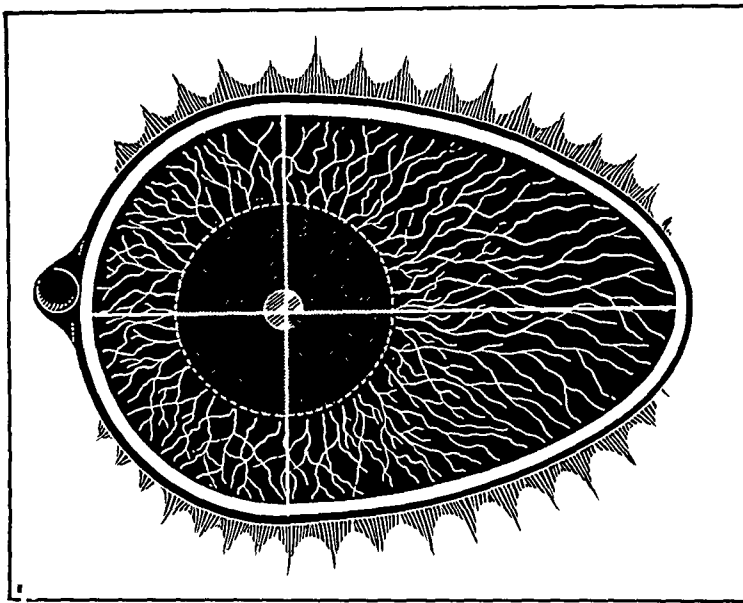


Fig 1—Division of the lens into four quadrants

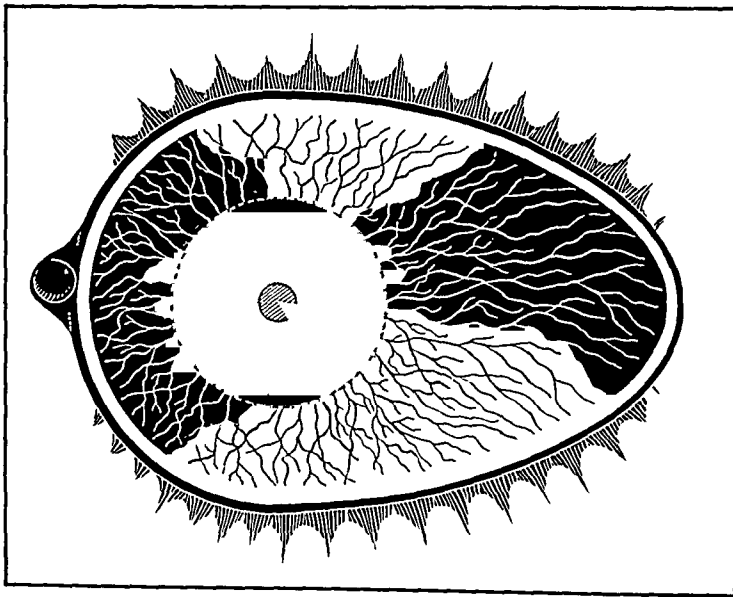


Fig 2—The ideally fitting lens

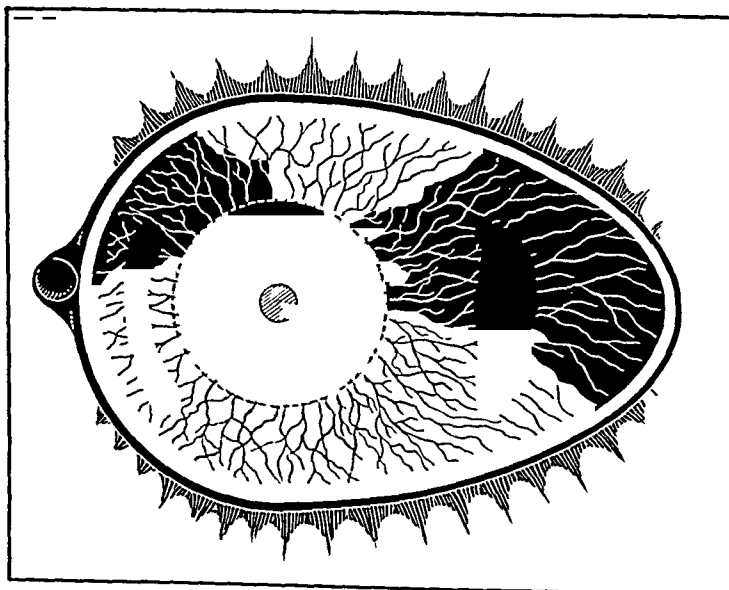


Fig 3—Tight areas in the nasal and temporal portions of the lens

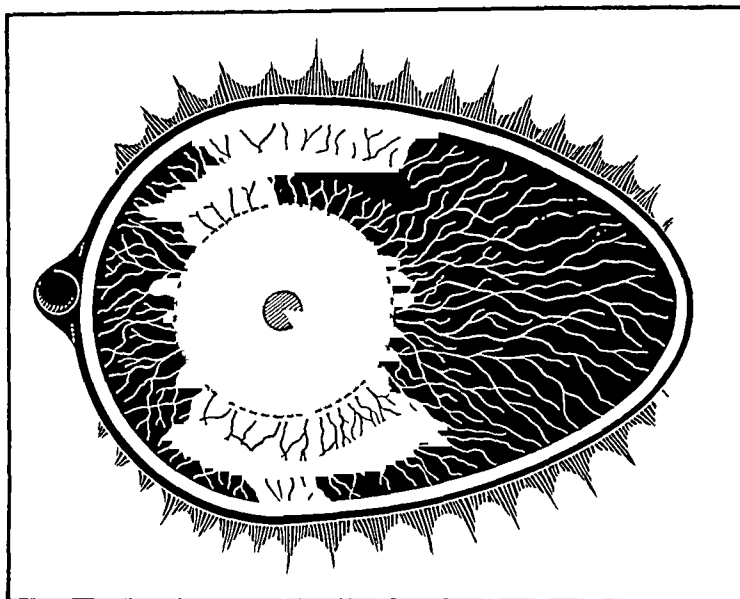


Fig 4—Tight areas in the lens above and below the horizontal line

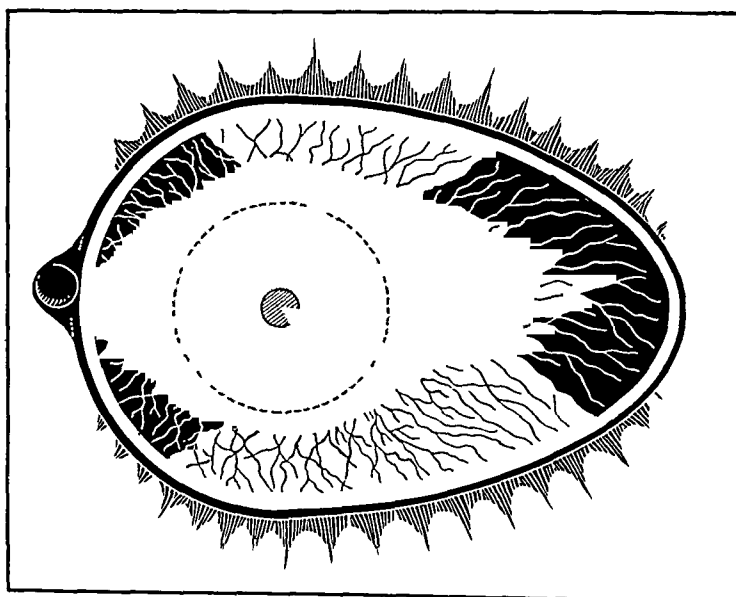


Fig 5—Fluorescein pools beneath the nasal and temporal portions of the lens

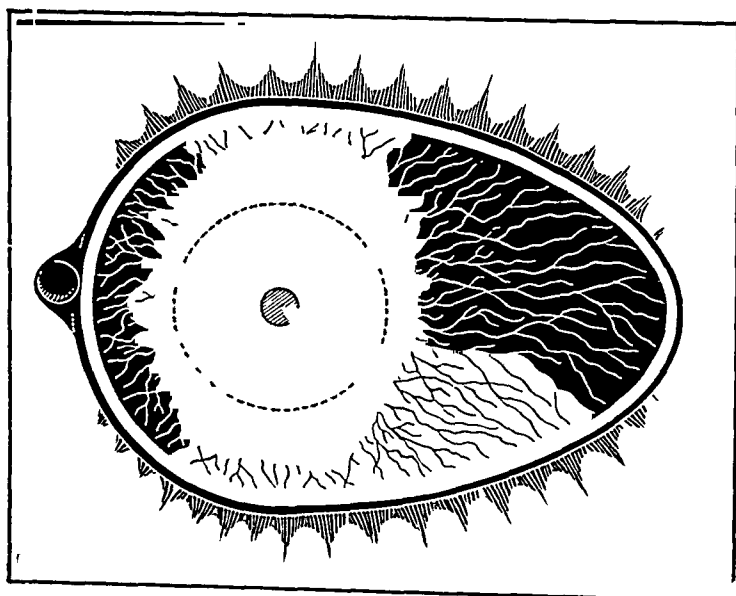


Fig 6—Fluorescein pools above and below the horizontal line of the lens

When he is making adjustments or corrections, the fitter should be guided by the following rules

RULE 1—If the lens is tight nasally and temporally, pressure is relieved on the temporal side first, except when the optical center is to the nasal side of the pupil, in which case pressure on the nasal side is relieved first. Pressure on the temporal side is relieved first in order to allow the lens to slide nasally and to prevent it from moving out of its proper position. Often when the temporal side is loosened, the area of pressure on the nasal side disappears. If the optical center of the lens lies to the nasal side of the pupillary center, then pressure on the nasal side is relieved first. The tight area on the temporal side will cause the lens to shift temporally. The optical center of the lens will finally coincide with the center of the pupil.

RULE 2—If the lens is tight above and below the horizontal line, pressure in the lower portion is relieved first, except when the optical center is higher than the pupillary center, in which case the upper portion is corrected first. Pressure in the lower portion is relieved first in order to allow the lens to slide upward. The pressure above the line will be lessened. If it does not disappear altogether, the corresponding area of the lens should be ground, but only after the lower area of pressure has been adjusted. Pressure in the upper portion is relieved first only when the optical center is above the pupillary center. If the upper portion is ground, the lower area of pressure will force the lens downward, and the optical center will coincide with the pupillary center.

Any isolated tight areas should be adjusted by the usual methods. When the tight areas are corrected, many of the loose areas will probably disappear. However, it is necessary to make a second fluorescein test for detection of any remaining loose areas.

CORRECTION OF LOOSE AREAS

Corneal contacts are caused by loose areas. If the lens does not rest evenly on the sclera, the loose areas allow the eye to move behind the lens, with the result that the lens strikes the cornea. Loose areas are detected by the infiltration of the fluorescein solution into the scleral portion, with the formation of pools. These pools must be eliminated when a corneal contact is present. If no corneal contact is observed, the loose areas need not be adjusted.

Elimination of the pools is effected by grinding of the portions of the inner surface of the sclera that do not show the presence of fluorescein—in other words, the regions surrounding the loose areas. This allows the lens to settle back, with the result that the pools are reduced in size and finally disappear.

RULE 3—If there are corneal contacts both nasally and temporally, the nasal pool is eliminated first, except when the optical center is to the nasal side of the pupil, in which case the temporal pool is eliminated first. By elimination of the loose areas at the nasal side first, the lens is allowed to settle at the nasal side, so that it is kept in its proper position, i. e., turned a little nasally, to allow for convergence. The loose area at the temporal side generally decreases in size, and, if necessary, the inner surface of the lens around this area may be ground.

RULE 4—If there are corneal contacts both above and below the horizontal line, the upper pool is eliminated first, except when the optical center is higher than the pupillary center, in which case the lower pool is eliminated first. If the upper pool is eliminated first, the lens will settle into position, so that the slight drop due to gravity and the pressure of the lids are offset by an increase in the bearing surface of the upper part of the sclera.

Other Procedures—Rarely is there a corneal contact below the line. However, if one is present or the optical center is above the pupil, then the portion of the lens surrounding the lower pool is ground away. The lens will fit closer to the lower part of the sclera, and the optical center will move downward.

In cases of corneal contacts not covered by rules 3 and 4 the following procedures are in order:

1 When a single contact occurs, the region around the adjacent loose area is ground away.

2 At times a contact lens will seem to have a clearly defined fluorescein pool, as illustrated in the ideally fitting lens, and yet a corneal contact may appear. In such a case if the lens is moved gently in the direction in which the corneal contact appears, a slight infiltration of fluorescein into the scleral section will be noted. This indicates a loose area. This area should be marked and the portion surrounding it ground off until the lens settles in position, with elimination of the corneal contact.

3 When the periphery of the lens stands away from the sclera, the edges should be tightened. This is accomplished as follows: The lens is placed over the cast (dental stone positive), the loose area is marked on the cast, and then some of the dental stone is removed with a knife and the marked area smoothed with sandpaper. The lens is replaced on the cast. A dental wax spatula is heated over an alcohol lamp. The tool is placed on the loose area of the lens, and a rocking motion is used. The tool is not removed until it has completely cooled. This procedure is repeated until the loose area has been eliminated. The tool is not allowed to become too hot, as it will soften the material.

NEURODERMATITIS WITH CATARACT

REPORT OF TWO CASES

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From 1101 to 1921 there were no American reports on the syndrome of cataract associated with neurodermatitis. In the European literature, however, Rothmund,¹ in 1868, described the occurrence of cataract in connection with changes in the skin. Andogsky² used the term "cataracta dermatogenes" in describing a case of bilateral cataract with an associated cutaneous eruption. Similar cases have been reported by Lowenstein,³ Gault,⁴ Winkler⁵ and others.

The first report in the English language was that of Davis,⁶ who, in 1921, described the case of a 15 year old girl with neurodermatitis accompanied by cataracts, which matured in one year. Daniel,⁷ from the Mayo Clinic, in 1935, reported 3 cases and mentioned the importance of a family history of allergy.

At first it was generally considered that the "neuro" part of the name alluded, perhaps, to some disturbance along the course of the nerves, actually, it refers to the unstable sympathetic system and emotional background of the patient. The papular rash is distributed over the face, neck, chest and flexor surfaces. The skin becomes ichthyotic and thickened, as though covered with a layer of shellac. Intense itching is the chief symptom. The endocrine system frequently seems to play a definite etiologic role. Epinephrine, thyroid, parathyroid and pituitary extracts have been reported of value in treatment in some cases. Brunsting⁸ stated

Those who wish to preserve the concept of a primary nervous instability as an important part of the background in cases of these disorders still cling to the term "neurodermatitis."

He further stated

One cannot deny that the elements of chronic fatigue and nervous imbalance must be considered in the proper control of this disorder, but it does not seem likely in my opinion that the nervous background is primarily responsible for the syndrome.

He apparently believed in the existence of a certain allergic factor, and this opinion was strengthened by the frequent family history of allergy and by the fact that of his 101 cases, cataract was present in 10 and the average eosinophil count was slightly over 9 per cent.

1 Rothmund, A. Ueber Cataracte in Verbindung mit einer eigentumlichen Hautdegeneration, Arch f Ophth (pt 1) **14** 159-182, 1868.

2 Andogsky, N. Cataracta dermatogenes, ein Beitrag zur Aetiologie der Linsentrübung, Klin Monatsbl f Augenh **17** 824-831, 1914.

3 Lowenstein, A. Katarakt bei Neurodermatitis, Klin Monatsbl f Augenh **72** 653-657, 1924.

4 Gault, N. Cataracte névrodermitique, Bull Soc d'opht de Paris, 1933, pp 280-284.

5 Winkler, A. Beitrag zur Genese der Cataracta dermatogenes, Arch f Ophth **139** 526-531, 1938.

6 Davis, W T. The Relation of the Eye and Certain Skin Diseases, South M J **14** 237-241, 1921.

7 Daniel, R K. Allergy and Cataracts, J A M A **105** 481-483 (Aug 17) 1935.

8 Brunsting, L A. Atopic Dermatitis (Disseminated Neurodermatitis) of Young Adults. Factors in One Hundred and One Cases and Report of Ten Cases with Associated Cataracts, Arch Dermat & Syph **34** 935-957 (Dec) 1936.

The following 2 cases illustrates the syndrome of neurodermatitis associated with cataract

REPORT OF CASES

CASE 1—A white youth aged 18 years was first examined on March 22, 1937. He had complained of poor vision in both eyes for one year.

Family History—His mother had suffered from Meniere's disease for the past five years, his father was living and in good health. He had 1 sister, aged 10 years, who was healthy.

Personal History—Birth was normal. Asthmatic attacks began at the age of 5 months and continued to recur for ten years. Eczema appeared at the age of 5 years. He had the usual diseases of childhood, as well as two attacks of otitis media. He stated that he was extremely allergic. During the entire time he was under my care he proved to have a decidedly emotional temperament.

Examination showed that vision in each eye was 20/65, unimproved. Five weeks later this had decreased to ability to see hand movements with the right eye and to 20/200 in the left eye. The eyelids were brawny, the conjunctivas were normal. Each eye showed anterior and posterior cortical opacities in the lens, a clear nuclear area remaining. The reflex from the fundus of each eye was pink, with imperfect details. Tension was normal in each eye.

In May 1937, an extraction of the cataract was performed on the right eye through a subconjunctival stereocorneal incision made with a keratome. The lens proved to be soft throughout. No sign of a nucleus was observed. Recovery was uneventful. Corrected vision was 20/13.

By July 1937, vision in the left eye had decreased to counting of fingers at 2 feet (60 cm). On Oct 25, 1937 the cataract was extracted by the method already described. The result was corrected vision of 20/13.

When the patient was last examined, on Oct 14, 1942, corrected vision in each eye was still 20/13. The cutaneous condition had improved, there being less itching and redness.

CASE 2—A white woman aged 23 was first examined on July 23, 1937. She had been told six or seven years ago that cataracts were developing. She stated that for four or five years she had received roentgen therapy. These treatments were discontinued two years prior to my seeing her. During the latter period glandular extracts and concentrated vitamin preparations were administered.

Family History—There was a history of nervous instability in both parents.

Personal History—When the patient was 11 years old, eczema first appeared under the arms, resembling multiple boils. In the course of one year a similar lesion broke out on the neck and face. Asthmatic attacks began at the age of 13 years and still continued. The usual diseases of childhood occurred. Many tests for allergy showed a positive reaction. Her menstrual cycle was always normal except for one period of suppression during the roentgen treatments.

Ocular Examination—**Right Eye**. The lids were thickened, brawny and ichthyotic. The conjunctiva was slightly congested. There was a keratoconus with a dense opacity in the lower quadrant, due to breaks in Descemet's membrane. The anterior chamber was deep. From its milky appearance the cataract appeared to be hypermature. Vision was limited to ability to see hand movements.

Left Eye. The lids and conjunctiva showed a picture identical with that in the right eye. There was also a keratoconus with a dense opacity, due to breaks in Descemet's membrane. The cataract was immature. No details of the fundus could be observed. Vision was 20/100, unimproved.

Tension in both eyes taken with the fingers because of the keratoconus, was high normal. This was reduced to normal by use of pilocarpine.

Operations—On April 3, 1939 a linear extraction was performed on the right eye, the same method being employed as that described in case 1. The cataract was found to be very soft throughout, so that it was readily removed by irrigation. Recovery was uneventful. Corrected vision was 20/50, that it was not better was due to the keratoconus.

On April 8, 1942 a similar linear extraction was performed on the left eye. Recovery was somewhat delayed, probably owing to an exacerbation of the eczema elsewhere in the body. On the last examination, Oct 23, 1942, corrected vision was 20/65, a little less than that in the fellow eye, because the corneal scars were denser.

SUMMARY

1 The patients whose cases are reported were both emotionally unstable and reacted positively to many different tests for allergy

2 The skin of the eyelids of each patient was brawny, red and itchy, with no involvement of the cilia, as has been reported by some observers

3 The conjunctiva was not involved except in 1 case, in which it was slightly inflamed

4 Both the patients were young persons whose cataracts developed during the active stage of eczema and neurodermatitis

5 Both patients belonged to the white race

6 In each patient, after the first definite evidence of opacities in the lenses, the maturing process was rapid

7 There was no undue postoperative reaction, except for the trivial effect in one eye, as previously explained

CONCLUSIONS

The absence of undue postoperative reaction after the removal of cataracts from both eyes of 2 patients in the active stage of neurodermatitis seems to indicate that such a condition lends itself well to surgical intervention and presents no more hazards than does cataract complicated by other diseases

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RETINAL DETACHMENT AND TRAUMA

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As Parsons succinctly put it, "The exact mechanism of detachment is not completely understood, indeed detachment of the retina is still one of the difficult problems of pathology" In other words, as it is not known how a detachment is produced, its relation to trauma must remain vague Yet one cannot but be struck by how generally the thesis of a traumatic origin is accepted For some time I have noted, in examining patients with retinal detachment, how rare a traumatic origin really is, and this has led me to review 400 successive cases in which I have had the opportunity to make examination

These 400 cases may be classified as follows ¹

Associated Condition	No of Cases	Percentage
Myopia	202	50
Trauma	52	12
Direct	32	
Indirect	20	
Hemorrhage (vitreous and retinal)	21	
Aphakia	37	9
Extracapsular extraction	23	
Intracapsular extraction	7	
Discission	7	

Cases of bilateral detachment numbered 58, or 14 per cent

The cases of myopia were represented in the etiologic groups as follows

Etiologic Condition	No of Cases	Percentage
Trauma		
Direct	10 in 32	33
Indirect	15 in 20	75
Aphakia		
Extracapsular extraction	11 in 23	45
Intracapsular extraction	1 in 7	14
Bilateral	32 in 58	55

The degree of myopia was over 10 D in 25 per cent, from 5 to 10 D in 42 per cent and up to 5 D in 33 per cent of cases The danger of detachment gradually increased with the degree of myopia up to a certain point and was greatest between 8 and 16 D of myopia Detachment occurred with the greatest frequency in persons between 45 and 60 years of age, when nutritional disturbances occur in the ocular tissues The incidence of trauma decreased as the degree of myopia increased Direct injury was more frequent in cases of hypermetropia than was indirect injury Spontaneous detachment was the rule in cases of myopia

It seems reasonable to divide cases of traumatic detachment into those in which the detachment occurs in previously healthy eyes and those in which it occurs in previously defective eyes and to classify the traumas as direct and indirect The

Read before the American Ophthalmological Society, Hot Springs, Va, June 11, 1943

¹ The figures in the tabulation do not add up to 400, as the number of cases of hypermetropia was omitted, and in a considerable number of instances the refraction was not indicated The real number of cases of myopia was unquestionably much greater than 202

types of trauma in this series of cases were the same as those usually indicated in the literature

Direct trauma generally resulted from direct blows to the eyeball with a ball, fist, stone or other hard substance. It occurred principally in cases of young persons. Myopic eyes did not preponderate. The types of lesions were the oral tear and round or giant holes, but the horseshoe-shaped tear was not observed. Although detachment of the retina can best be explained by contrecoup, choroidal and scleral ruptures were apparently caused by different, and probably more severe, injuries. Perforating injuries were excluded, as the detachment then results from lesions of the vitreous following hemorrhage or inflammation.

Indirect trauma was caused by severe blows to the head or body, succussion of the head or body, excessive bodily exertion, such as that in lifting, and excessive coughing or sneezing. The injury might be mild, such as that produced by rubbing the eyes with the fingers, long motor or railway journeys, fluid splashed in the eye, extraction of a tooth or removal of a foreign body from the cornea. Indirect injuries are in themselves vague, and the length of time between the alleged trauma and the onset of the detachment is indefinite. In my series of cases of indirect trauma the patient's age was generally above 40, the 2 youngest patients were each 29 years old. The refraction showed myopia in 15 cases and hypermetropia in 4 cases. The type of retinal tear was not characteristic, but there were no oral tears.

There can be no question about the traumatic origin of a detachment in young persons with normal eyes who have suffered severe injury to the eyeball and that of a detachment which follows a penetrating injury of the eyeball. The role of indirect injuries is more difficult to explain, especially the mild ones. To explain the relation between retinal detachment and indirect trauma a predisposition on the part of the eye is assumed, and it is believed that in the presence of certain changes in the eye (predisposition), a mild injury or a sudden circulatory disturbance on muscular exertion may be the determining cause of a detachment which is ready to develop, just as the detachment generally occurs without trauma.

The predisposition consists in certain changes in the eye which are present in myopic eyes and make such eyes susceptible to retinal detachment. Among these, cystoid degeneration of the retina, first described by Leber and confirmed by Gonin, occurs in the external plexiform layer, with changes in the pigment epithelium, implying that the choroid is also affected. Clinical signs of inflammation are absent, and a local circulatory disturbance must be considered a factor. Vogt showed that similar changes occurred in the aging eye from nutritional disturbances, and Hanssen demonstrated tears and other changes in the retina in myopic eyes without detachment of the retina.

The vitreous, also, takes part in this degeneration and undergoes fluidification, shrinkage and detachment. Gonin, in his microscopic study of eyes with retinal detachment, found that the vitreous was always shrunken from one third to one half of its former size, and this observation has been confirmed by other investigators (Lister, Lindner and von Sallmann). The presence of a detachment of the vitreous has been recognized clinically by several investigators (Benziger, Pillat, Lindner, von Sallmann and Vogt).

Adhesion of the vitreous framework to the retina occurs in healthy eyes at the base of the vitreous and has been observed on histologic examination in places in which the vitreous is adherent to the retina, where the greatest changes in the retina exist and where the hole in the retina is situated. The presence of this adhesion to the margin of the hole has been observed on clinical examination with the slit lamp by Bock.

Finally, as the vitreous body was known to move with movements of the eyeball (Best), it seemed logical to a number of investigators that this movement can easily cause traction on the retina and that if the retina is weakened a tear results and conditions necessary for the development of the detachment are present (Leber, Gonn, Lindner and others)

If the same histologic changes explain the onset of spontaneous and of traumatic detachment, it is impossible to draw a sharp line between the two types. If movements of the vitreous are accepted as a factor in the causation of spontaneous detachment, they can, all the more, explain the mysterious detachment after an indirect trauma. Anything, therefore, which will cause movements of the vitreous can produce a detachment in a predisposed eye. But Lindner showed in his experiments that it is not just a shaking of the eyeball that produces a detachment but that the force must be of a rotating or whirling nature. The question arises: Under what conditions does the eyeball undergo ocular rotation? It has been suggested that with indirect trauma the patient instinctively makes a rapid protective movement of the eyes, whereby the vitreous drags on the upper half of the retina and causes a rupture of the retina.

Kruckmann² reported the cases of 3 young persons with emmetropia who were carrying heavy weights, the weight slipped, the body straightened, and the eyes were forced upward and strongly abducted. On the following day a detachment was present, in the lower temporal quadrant, which the author explained on the basis of retinal swelling, following sudden ischemia, similar to cerebral swelling. The location is explained by action of the inferior oblique muscle, which suddenly contracted when the eyes were raised. This produced aspiration of the sclera with vacuum action on the retina. Kruckmann also considered the role of muscular action in the development of detachment in cases of indirect trauma. The muscles that came under consideration were the two oblique muscles, as these are the only muscles whose insertion on the sclera covers an area of the sclera and choroid beneath which retinal tissue is situated directly. In the aforementioned cases the inferior oblique muscle was regarded as the active factor. This condition, according to Kruckmann, differs from the tears in the retina which occur in the insertional area of the superior oblique muscle in the myopic eye and are explained by uneven traction of that muscle because of its peculiar anatomic structure and insertion.

Bartels³ drew attention to the role of the superior oblique muscle in explaining the prevalence of retinal holes in the superior temporal quadrants.

MacDonald⁴ suggested that a hydrodynamic phenomenon may cause detachment of the retina in persons who do heavy lifting. The transmitted intracranial pressure obstructs the central retinal vein, and the excess fluid from the choroidal exudate and the central retinal artery collects in the retina and the intraretinal space, with resulting detachment.

Walker⁵ raised the interesting question why detachment occurred in only one eye when the injury was general and gave a reason for the frequency of retinal tears in the upper temporal quadrant. This frequency the author explained by the statement that the retina in the upper temporal quadrant is under additional mechanical disadvantage, pressure and vacuum action, as the superior oblique

2 Kruckmann, E. Netzhautablosung und indirektes Trauma, Ber u d Versamml d deutsch ophth Gesellsch **51** 304, 1936

3 Bartels, M. Ueber die Entstehung von Netzhautablosungen, Klin Monatsbl f Augenb **91** 437, 1933

4 MacDonald A. E. Etiology of Idiopathic Retinal Detachment, Am J Ophth **21** 658, 1938

5 Walker, in discussion on MacDonald,⁴ p 661

muscle is exposed to peculiar punishment, which is greatest in the eye acted on most strongly by its superior oblique muscle in the conjugate positions

Friedman,⁶ in an article on traction on the optic nerve as a force in production of retinal detachment, spoke of (1) the movements of the vitreous in rapid movements of the eye as related to the phenomenon of inertia and (2) pressure on the globe by the extraocular muscles, which is transmitted to the retina. The latter factor was suggested by the frequency of tears in the region underlying the superior oblique muscle, which is being constantly used in all close work. The author concluded that both these factors act on the retina during ocular rotation and that the use of stenopaic goggles is sound.

Perhaps when more is known about detachment of the retina, the problem of its relation to indirect trauma will be explained. There are still many problems concerned with this subject. With the appreciation of the significance of the retinal hole other important features may be overlooked. Some investigators, especially Kummell, have claimed that it is not the hole alone which causes detachment but that changes in the hydrostatic equilibrium between the preretinal and the retroretinal spaces, from reduction in vitreous pressure, constitute an important contributing factor and should not be disregarded. Attention has repeatedly been drawn to the fact that in many cases contusion does not lead to detachment even in myopic eyes and that detachment is not observed after strenuous gymnastic exercises or in association with fractures of the skull or war injuries, and that while severe bodily exertion is common, resulting detachment is unusual. Though the cause of the detachment after indirect trauma is difficult to define, the question of the relation cannot be dismissed as irrelevant when such careful observers and scientific investigators as Gonin, Vogt and Jeandelize are firm believers in the role of indirect trauma. At the same time, all persons are inclined to find a cause for an accident, especially if compensation is a factor. A guiding rule in the estimation of the cause would be that the exertion must be greater than usual and that the symptoms of detachment should promptly follow. Davidson,⁷ who had a large experience with compensation claims, stated that the association of trauma and detachment could be accepted only when the visual disturbance was complained of within two days after the injury and the detachment developed before the end of two weeks.

In a review of this series of cases of detachment in their relation to trauma, two other points become apparent and are, I hope, worthy of mention. The first is bilaterality of retinal detachment. This was present in 58 cases, or about 14 per cent, in 32 of which, or 55 per cent, myopia was represented. The feature of bilaterality is significant and speaks against a traumatic origin. The cases of bilateral detachment can be divided into cases involving juveniles and cases involving myopic persons and the aged. While the detachments were bilaterally symmetric in the young, in the other patients there was no symmetry. The cause was general, and the important factor was the local condition in the eye. A careful examination of the fellow eye in all cases of detachment is always important (Sourdille).

The second point of significance is the association of detachment with aphakia. There is still a great deal to be learned about this relation, and I shall refer only briefly to it here. Retinal detachment in aphakic eyes is related to trauma only in its widest sense, as with perforating injuries of the eyeball, there are set in motion changes in the intraocular structure, especially in the vitreous, which after some

6 Friedman, B. Mechanics of Optic Nerve Traction on the Retina During Ocular Rotation, *Arch. Ophth.* **25** 564 (April) 1941.

7 Davidson, M. Netzhautabhebungen infolge indirekten Traumas, vom Standpunkt des Arbeitsunfallgesetzes, *Tr. internat. Ophth. Cong.* **4** 201-203, 1933.

time lead to detachment. The aforementioned predisposition and the loss of vitreous at operation are undoubted factors, though the quantity of the vitreous lost is not the essential feature.

Detachment of the retina was observed in 37 cases of aphakia, of which extracapsular extraction had been performed in 23, intracapsular extraction in 7 and discission in 7. No deductions can be drawn from these figures, especially with respect to the relative frequency of retinal detachment after extracapsular and intracapsular extractions. Detachment of the retina after operation for congenital or lamellar cataract (discission, or needling) occurred in 6 cases, and in 1 case the operation was performed for high myopia. Shapland⁸ drew attention to the frequency of detachment after discission of soft cataract in a report on 50 cases of detachment associated with aphakia, in 22 of which needling for soft cataract was performed. The detachment occurred after an average interval of twenty-four and six-tenths years. Of 40 eyes with congenital cataract in Shapland's series, detachment occurred in 33. The bad prognosis he ascribed to progressive myopia, and no benefit resulted from operation for the detachment. Moore⁹ gave it as his opinion that removal of a lens, whether by extraction or by discission, predisposed to the development of detachment of the retina, and this in no negligible degree. Detachment occurred more frequently after the needling operation for soft cataract, and this, he suspected, was because of the prospect for so much longer life after this operation than after the usual extraction for hard cataract. Moore was so impressed by the poor prognosis of the needling operation for young patients that he doubted the wisdom of removal of both lenses for lamellar cataract unless the opacity was so dense that the eye was of little value if the operation was not done.

10 East Fifty-Fourth Street

⁸ Shapland, C. D. Retinal Detachment in Aphakia, *Tr Ophth Soc U Kingdom* **54** 176, 1934.

⁹ Moore, F. Diathermy in Ophthalmology, *Tr Ophth Soc U Kingdom* **53** 487, 1933.

Clinical Notes

PLASTIC SHELL FOR USE IN THE SIMPLE EVISCERATION OF THE GLOBE

SANFORD R. GIFFORD, M.D., CHICAGO

After many years of experience with Harold Gifford's method of simple evisceration of the globe, the only disadvantage which I have noted, when proper indications are observed, is the occurrence of conjunctival chemosis. It will be remembered that the operation consists in an incision across the cornea and into the sclera at each side, removal of the ocular contents by an evisceration spoon and careful wiping of the inside of the scleral shell with sponges to remove all uveal tissue. The entire cornea is retained. No sutures need be employed, or, at most, one suture between the lips of the corneal wound to keep them from overlapping during the healing process may be used. No implant is employed. The normal attachments of the conjunctiva are not disturbed, and, as a result of the trauma of evisceration, fluid tends to collect within and beneath the conjunctiva. This



Plastic shell for use in the simple evisceration of the globe

chemosis may be severe, to the extent of protrusion between the lids, a phenomenon alarming to the patient.

Various means have been tried to combat this complication, the most effective being the constant use of finely cracked ice in a rubber glove and a pressure dressing. To be effective the pressure dressing must be applied either constantly, which excludes the use of ice, or every night, while the ice is not in use. In spite of these measures, or because of the difficulties in carrying them out rigorously in practice, difficulty with chemosis continued to occur not infrequently.

Hence an attempt was made to exert even pressure on the conjunctiva by some form of shell. Several experiments resulted in the shell shown in the figure¹. This device resembles in shape a shell prosthesis, it measures 24 by 20 mm in frontal dimensions and has a curve 7 mm in depth. The shell is made with either white or transparent plastic material, the latter having the advantage that the stump may be observed without removing the shell. The same shell will fit either eye, and one of the dimensions given has been found to fit nearly all patients without difficulty. This includes children as young as 8 years. With infants it would be necessary to employ a smaller shell. The shell is inexpensive and may be sterilized in alcohol or in Bard-Parker solution² so that it may be used by more than one patient.

The shell is inserted on the operating table at the end of evisceration, and ice is applied in the usual manner through a single layer of gauze during the daytime.

From the Department of Ophthalmology, Northwestern University Medical School

¹ This shell is made by Mager and Gougelmann, 30 North Michigan Avenue, Chicago

² The composition of the Bard-Parker solution is as follows: ethyl alcohol, 67.8 per cent, methyl alcohol, 9.3 per cent, formaldehyde, 8 per cent, and water, 14.9 per cent.

for one week after operation. With the shell in place it is not necessary to apply pressure at night, since the pressure of the lids on the shell prevents the occurrence of chemosis. The shell is easily removed for dressings by the suction cup used for insertion of contact glasses, but in the case of children it has proved practical to leave it in place for two weeks, at which time the first prosthesis may be fitted. Use of the shell is continued usually for this length of time, as if it is removed sooner chemosis may develop. It is usually best to postpone the fitting of a permanent prosthesis for at least two months, since slight changes in the shape of the stump occur during this time.

In addition to preventing chemosis, the shell holds the sclera and the cornea in correct position, so that the tissues are allowed to shrink uniformly. The impression has been gained that the stump is more regular and a little larger when the shell has been employed than when pressure has been applied without a shell.

In addition to its use after evisceration, employment of the shell is of advantage after enucleation with an implant in Tenon's capsule, an operation which may be followed by considerable chemosis. The additional use of a pressure dressing for two weeks is considered of great importance, however, after any implantation, to prevent displacement of the implant.

720 North Michigan Boulevard

BILATERAL METASTATIC CARCINOMA OF CHOROID

Report of a Case

GEORGE MARTIN McBEAN, M D, CHICAGO

Bedell,¹ in a report of a case of bilateral metastatic carcinoma of the choroid, stated that only 250 cases of this condition have been recorded. It is late to record such a case which I encountered in 1916, but because of its rarity it should be listed.

Miss G D, aged 52, white, a schoolteacher, had had both breasts removed for carcinoma, with recurrence of the neoplasm about the right clavicle, for which she was undergoing roentgen therapy.

The right eye showed an area of episcleritis on the temporal side and the fundus a pale gray zone, about the size of the disk and slightly elevated, under the insertion of the external rectus muscle. There was a scintillating scotoma, but the field otherwise was not contracted. Two weeks later severe pain developed about the right eye and the right side of the head, a subconjunctival hemorrhage also appeared while she was in the hospital under the surgeon's care. He had ordered instillation of atropine. When I saw her the next day, the tension was elevated, and the media were too hazy to permit visualization of the fundus. The tension (Schiotz) was plus 60. Miotic drugs were instilled, and a paracentesis was done. Dr Cassius Wescott examined her with me in consultation, and later we did an iridectomy. Although tension was reduced, severe pain recurred, the eye became blind, and enucleation was done. Dr E V L Brown and Dr Francis Lane, who studied the eye, observed the tumor under the insertion of the external rectus muscle.

Metastases occurred later in other regions of the body, including the femur of one leg, which underwent spontaneous fracture. Shortly before the patient died, I examined the left eye, which was becoming blind, and found a wide retinal detachment covering a solid growth. Enucleation was not permitted either before or after death, but I believe this eye was also the seat of a metastatic carcinoma.

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¹ Bedell A I. Bilateral Metastatic Carcinoma of the Choroid, Arch Ophth 30 25 (July) 1943

Ophthalmologic Reviews

EDITED BY DR FRANCIS HEED ADLER

LOCAL ANESTHESIA IN OPHTHALMOLOGY

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The aim of this article is to assemble and make easily available the more generally accepted methods of local anesthesia in ophthalmic practice. A few modifications that have been tried and found satisfactory are included.

HISTORICAL REVIEW

Anesthesia has unquestionably been one of the great factors in the evolution of modern surgery and is, in a large measure, responsible for the tremendous advance that has been made in surgery since 1846, when it was introduced. It is difficult to picture surgery without the aid of anesthesia, but this was the situation less than one hundred years ago. In spite of the fact that the desire to prevent pain during surgical operations dates back to antiquity, this aim was not realized until comparatively recently.

The early Egyptian, Chinese, Greek and Roman physicians attempted to allay the pain incident to surgical operations by the use of alcoholic beverages, drinks with narcotic properties and inhalations of narcotic drugs. In medieval times the *spongia somnifera*, or "sleep sponges," were very popular and were rather generally used in an attempt to produce surgical anesthesia. In the "Antidotarium" of Nicolaus Salernitanus an interesting account of these sponges is given:

Take of opium of Thebes one ounce, juice of hemlock, poppy capsules, juice of mandragora, juice of wood-ivy, of each, one ounce. Put all these into a vessel together with a new sponge which is just as it came from the sea and has not been in contact with fresh water. Place the vessel in the sun during the dog-days until the sponge is needed, moisten it with a little hot water and apply it to the patient's nostrils, and he will quickly fall asleep. When you wish to rouse him, apply the juice of fennel-root, and he will soon wake.

This prescription expresses all the confidence of modern advertisements. The use of these "sleep sponges" was gradually discontinued because in doses sufficiently large to produce narcosis the drugs were distinctly dangerous and in smaller quantities the results were disappointing. Also, as suggested in the "Bibliotheca Osleriana," the sponges were abandoned partly because of the introduction of the tourniquet for amputations and operations on the extremities.

The ophthalmologic portion of the "Tetrabiblion" of Aetius of Amida (502-574 A D), which covers rather fully the ophthalmology of the ancients, makes no mention of any attempt at anesthesia in surgical operations. In chapter LXVIII, in discussing the operation for trichiasis, he commented "As, however, a few patients, because of cowardice, can never bring themselves to take an operation." This, with similar references, leads one to believe that, in lieu of anesthesia, the ancients relied principally on stalwart assistants to secure a quiet, if not a relaxed, patient. That the patients were not always quiet is evident from another statement, regarding the operation for pterygium, in which Aetius remarked that care must be observed in order to avoid cutting the lids.

This review is a revision of a candidate's thesis for membership in the American Ophthalmological Society (Local Anesthesia in Ophthalmology, Tr Am Ophth Soc 32:399, 1934).

These operations are mentioned particularly because of the historical interest they possess. However, enucleation with local anesthesia did not meet with general approval, probably owing to the alarming toxic effects that followed the strong solutions of cocaine used.

Some years later enucleation with local anesthesia was revived by Siegrist,¹¹ Lowenstein,¹² Seidel¹³ and others, a weaker solution of cocaine, procaine or a similar substance being used. At present enucleations are done easily and painlessly with the use of local anesthesia, and with many surgeons it is the procedure of choice.

Infiltration with cocaine near or into the nerves was first reported in 1884 by Hall,¹⁴ who observed that the tissues supplied by the nerves so treated became anesthetic. The technic of this procedure, which is now spoken of as nerve block, has been greatly improved and is in general use.

The toxicity of cocaine was quickly realized, but not until many unhappy results had followed its use, particularly in general surgery, in which larger quantities were used than in ophthalmic surgery. Many of the unfortunate accidents were probably due to the rapid injection and absorption of strong solutions of the drug.

Also, epinephrine had not yet been discovered. Cocaine still holds an important position in ophthalmic surgery, although in many procedures it has been replaced by less toxic and more efficient drugs.

After the discovery of the chemical composition of cocaine and its atomic grouping by Einhorn,¹⁵ the synthetic preparation of this alkaloid became possible. This served as a starting point for interesting experiments in which the anesthesiophoric atomic group was combined with new atomic groups. This chemical research resulted in the discovery of a number of new local anesthetics, such as phenacaine, eucaine and compounds of the orthoform group, and later of stovaine, amydrucaine, and procaine—certainly a triumph of an exact science.

In 1901 Takamine¹⁶ isolated the active salts of the adrenal gland and added epinephrine to the pharmacopeia. This contribution increased greatly the efficacy of local anesthesia and facilitated operative procedures in which considerable bleeding is encountered.

Until the introduction of ether, in 1846, the success of operations on the eye was largely dependent on the speed of the surgeon and the stoicism of the patient. Although the necessity for speed has long since been eliminated by the improved methods of both general and local anesthesia, some ophthalmic surgeons still extol the virtue of speed and place unwarranted emphasis and importance on it.

Such drugs as cocaine, ether and chloroform were known for years before their anesthetic properties were fully appreciated and used. So, also, much of the present knowledge of physiology and anatomy is allowed to lie dormant, and in the technic of local anesthesia many of the advances and improvements are not given the recognition that they deserve.

SENSORY DISTRIBUTION TO REGION OF THE ORBIT

Since the aim of anesthesia is to eliminate pain, a consideration of the distribution of pain sense in the different tissues with which the ophthalmologist has to deal seems a logical approach to the problem. No doubt the pain sense varies in different persons, as does the interpretation of pain by different surgeons. The literature

- 11 Siegrist, A. *Klin Monatsbl f Augenh* **45** 106, 1907.
- 12 Löwenstein, A. *Klin Monatsbl f Augenh* **46** 592, 1908.
- 13 Seidel, E. *Klin Monatsbl f Augenh* **49** 329, 1911.
- 14 Hall, R. J. *New York M J* **40** 643, 1884.
- 15 Einhorn. *München med Wchnschr* **46** 218, 1899.
- 16 Takamine. *Therap Gaz* **17** 221, 1901.

furnishes many examples of this, and the following case illustrates the point. An operation for the removal of a toe nail was reported by Shaw,¹⁷ who stated that after the toe was wrapped in cotton saturated with cocaine for a few minutes, the nail was divided and removed without pain.

According to Braun,¹⁸ the skin, with its innumerable nerve endings, is probably the most sensitive tissue in the body. Although the skin has a highly developed pain and tactile sense, which is more acute in some areas than in others, it can hardly be considered more sensitive than the cornea. One can easily demonstrate this by touching the skin and then the cornea with a wisp of cotton. However, the skin is extremely sensitive to pain, and if the surgeon is to retain the confidence of the patient, it is well for him to avoid causing unnecessary pain. In the introduction of the anesthetic agent, the pain caused when the skin is pierced may be practically eliminated if the skin is rendered insensitive by the production, first, of an intra-dermal wheal.

The loose subcutaneous tissue possesses little, if any, sensibility, although numerous conducting nerves containing sensory fibers for the skin traverse this area. One may produce pain by cutting or by making traction on these nerves, but, as a rule, no pain will be experienced when a needle passes through the subcutaneous tissue unless it comes in contact with one of the small sensory nerve trunks.

In this respect, the orbital tissue corresponds to the subcutaneous tissue, and the introduction of a needle, as in orbital injections, is practically painless if the skin has first been anesthetized by the production of a small intradermal wheal, provided the periosteum is not pricked with the needle and the muscles and nerves are avoided.

The nerve distribution in muscles is practically the same as that in connective tissue, so that very sharp pain is caused if the sensory nerves are touched. However, if the nerve is not encountered, a needle may be introduced into healthy muscle tissue without its causing pain. Muscle fascia and the surrounding connective tissue are distinctly sensitive, so that if the needle is passed through these tissues without the parts being first anesthetized pain is experienced.

Tendon tissue appears to be without sensibility. However, the connective tissue covering the tendon and the tendon sheaths possesses a varying degree of pain sense. Joint capsules, ligaments, synovial membranes and periosteum are extremely sensitive, and if they are pricked by the needle considerable pain may be produced. There seems to be some difference of opinion with regard to the sensitivity of the bones, but in general they can be considered as having little pain sense. This is not true of the medulla of long bones, in which, however, sensibility is not acute. Cartilage is insensitive, but the perichondrium is well supplied with nerves and is very sensitive to pain.

Since the margins of the eyelids are richly supplied with sensory nerves, they are the most sensitive part of the lids. Although the conjunctiva and the cornea are extremely sensitive, they can easily be rendered insensitive by the instillation of a few drops of an anesthetic agent if the eye is not red and inflamed.

MENTAL ATTITUDE OF THE PATIENT AND THE SURGEON

In operations performed with local anesthesia, particularly ophthalmic procedures, the proper mental attitude of both the patient and the surgeon is so

¹⁷ Shaw. New York M. J. 40:588, 1884.

¹⁸ Braun,⁴ p. 29.

important that a consideration of this subject seems warranted. Often the entire important procedure of the production of anesthesia is consigned to the assistant or to the intern, and quite properly too, provided he has been instructed adequately and is sufficiently familiar with the technic. In visiting large clinics one occasionally sees a patient who is so frightened by the preliminary preparation that the surgeon finds it difficult to quiet him and to regain the confidence necessary to obtain his full cooperation.

Apprehension is usually the greatest cause of suffering before the operation. In order to assure the patient that every precaution will be taken to insure his safety and comfort, it is necessary to inspire confidence, and the surgeon who can obtain this rarely encounters a patient who "behaves badly." The patient is vitally interested in having a successful result, so if he does not cooperate, it is frequently the fault of the surgeon. Certainly, in most instances, the surgeon begins with the advantage of having the patient's confidence, otherwise he would not have entrusted his most valuable possession, sight, to that surgeon. The operator should strive to strengthen this confidence and endeavor in every way possible to avoid undermining it. The aim of all surgeons is to secure good results. With operators of equal surgical skill, the one who gains the patient's confidence will undoubtedly have the greatest number of good results.

Local anesthesia demands and allows deliberation and care in all the manipulations of the operator. A confident, orderly atmosphere in the hospital, particularly in the operating room, and a comfortable, well padded operating table invite complacency. In the preparation of the patient, careful attention should be given to the minor details. Patients are particularly sensitive at this time, so that the instillation of a drop without warning or the accidental introduction of soap, iodine, or the like, in the eye greatly upsets the patient's equilibrium. Hurried or inefficient attempts to produce anesthesia may inflict unnecessary pain. Even the slightest needle prick will, in certain patients, cause considerable pain, for at the time the anesthetic is introduced the patient is most apprehensive, his sensitivity to pain is greatly exaggerated and each succeeding needle prick seems to be of increasing intensity. It is, therefore, of the greatest importance to induce anesthesia painlessly in order to retain and strengthen the patient's confidence.

Haste should be avoided, and the operation should not be attempted until complete anesthesia has been secured. Any complaint of pain usually indicates the inefficient administration of the anesthetic rather than a defect in the anesthetic procedure, the anesthetic agent or the patient. It is best not to proceed with the operation until complete anesthesia is obtained, and then it will rarely be necessary to resort to the well known "vocal anesthesia." For the surgeon to scold and blame the patient, the assistants or the nurses or to charge the failure to faulty instruments indicates usually a lack of self control on his part.

With a limited number of patients the temperament or mental makeup offers difficulties. Patients undoubtedly differ to as great an extent in their mental as in their physical characteristics, so they must be approached as differently as one would approach the various surgical conditions encountered.

In many cases fear is the chief barrier that prevents one from operating on children with the use of local anesthesia. An experienced nurse who has won the confidence of a child can often engage its attention with interesting conversation, which allows the operation to proceed smoothly. Often with adults, if the attention of the patient can be diverted, the operation will be easier and pleasanter for all concerned. Remarks such as "Did that hurt?" or "We are almost finished" should certainly be avoided.

While the use of a sedative or hypnotic, such as one of the barbituric acid group, before operation aids greatly in giving one a confident, quiet and complacent patient, it is, nevertheless, of secondary importance and should be considered only as an aid. Sedatives of the barbituric acid group have the added value of counteracting to some extent the toxic action of the anesthetic agent.

AGENTS FOR LOCAL ANESTHESIA

Since the advent of cocaine, chemists have produced numerous substitutes, some of which have in large measure replaced cocaine, particularly in cases in which the anesthetic is injected for block or infiltration anesthesia. A consideration of all the local anesthetic agents is obviously unnecessary. Only a few of the more generally accepted ones which are particularly suited to ophthalmic surgery will be considered.

Instillation Anesthesia—For instillation anesthesia, cocaine, phenacaine (holocaine), butacaine (butyn) and tetracaine (pontocaine) are the agents most frequently used.

Cocaine Cocaine hydrochloride is the salt of cocaine that is generally used as an anesthetic agent. It is a white, crystalline powder, readily soluble in water and in alcohol. According to the report of the Committee on Local Anesthetics in Ophthalmic Work of the American Medical Association,¹⁹ cocaine may be sterilized by boiling without impairment of its efficacy. Braun²⁰ stated that no material loss of cocaine follows a single, rapid boiling of a small quantity of the solution, whereas repeated boilings of large quantities cause a diminution in the cocaine content, with diminished activity of the solution.

To prepare a fresh sterile solution of cocaine, Mikulicz recommended that the cocaine be dissolved in alcohol in a sterile flask stoppered with cotton and that when the alcohol evaporates sterile water or saline solution be added to the residue. According to the aforementioned report,¹⁹ the addition of 5 grains (0.325 Gm.) of boric acid powder to each ounce (29.5 cc.) of solution tends to preserve the solution, so that it will remain active longer.

The physiologic action of cocaine is that of a protoplasmic poison. It paralyzes temporarily, and without permanent damage, the sensory and motor peripheral nerves, and if brought into direct contact with sensory or motor fibers, it causes them to lose their power to transmit impulses. The sensory fibers are affected more quickly and easily than the motor fibers.

It is generally agreed that for infiltration or block anesthesia there are safer and better drugs than cocaine. In referring to these types of anesthesia, Braun²¹ dismissed cocaine as follows: "Cocaine, at least in surgery, has become obsolete." Labat²² stated (page 39) that "cocaine has been practically discarded except for contact anesthesia of mucous membrane."

General cocaine poisoning will be considered only briefly, since such highly toxic drugs as cocaine are no longer accepted for infiltration or block anesthesia, and in the amounts used in ophthalmologic practice it would be unusual for toxic symptoms to develop from topical use of the drug. When toxic symptoms do appear, the chief disturbance occurs in the central nervous system, which is most sensitive to cocaine. In mild forms of poisoning, appearing shortly after the use of cocaine, there is a sudden, usually transient, attack of vertigo, which may become more severe, particularly if it is allowed to continue. Fainting, a small compressible pulse, cold

19 Report of the Committee on Local Anesthetics in Ophthalmic Work of the American Medical Association Trans. Sect. Ophth. A. M. A., 1921, pp. 297-298.

20 Braun,⁴ p. 93.

21 Braun,⁴ p. 184.

22 Labat, G. Regional Anesthesia, Philadelphia, W. B. Saunders Company, 1928.

sweat, irregular and difficult respiration, formication and cold extremities may be followed by loss of consciousness. The pupils become dilated and fixed. Vomiting is frequent. Severe poisoning usually begins with epileptiform convulsions, exophthalmos and loss of consciousness, death results from paralysis of the respiratory center.

The local application of cocaine causes contraction of the small capillaries and arteries, especially of the mucous membrane, resulting in localized ischemia, followed by congestion or dilatation of the vessels. While the newer agents for local anesthesia have an anesthetic action similar to that of cocaine, they do not cause ischemia.

For superficial or surface anesthesia, one instillation of a 4 per cent solution of cocaine hydrochloride produces adequate anesthesia in five minutes. For deep anesthesia, such as is required for cataract extractions, four instillations at three minute intervals is the procedure usually followed, and it produces the maximum effect in about fifteen minutes.

In addition to the anesthetic action on the eye, cocaine dilates the pupil and causes slight paralysis of accommodation. The corneal epithelium is also affected, becoming desiccated, particularly if the eyelids are not kept closed or the cornea is not kept wet with a solution of boric acid or some similar solution. The tendency of the patient to keep the eyelids open and not to wink after the use of cocaine increases the possibility of the occurrence of this condition. Cocaine also devitalizes the cornea, so that if the drug is used for cataract extractions, collapse of the cornea and delay in closure of the corneal wound are more frequently observed than with such anesthetic agents as butacaine and tetracaine. For this reason, cocaine is not so desirable for the operation of corneal transplantation, and its use may account for some of the grafts' becoming cloudy.

Cocaine hydrochloride is used in from 1 to 10 per cent solutions, but the 4 per cent solution is generally preferred. In operations on muscles some surgeons use powdered cocaine over the operative field. Except when its use is contraindicated, epinephrine is instilled in conjunction with the anesthetic agent, in order to constrict the vessels, decrease bleeding and prolong the anesthetic effect. Sollmann²³ stated that for surface anesthesia the addition of an equal volume of a 0.5 per cent solution of sodium bicarbonate to a solution of cocaine increases the activity of the cocaine one to two times.

Phenacaine. Phenacaine was prepared in 1897 by Taeuber by combining molecular quantities of acetophenetidin and phenetidin (ethyl ester of paraaminophenol). Although the basic compounds of phenacaine are insoluble in water, the hydrochloride of the drug is soluble up to 2.5 per cent and is the salt used. Phenacaine hydrochloride is incompatible with alkalis and their carbonate bases, so that porcelain instead of glass dishes should be used in its preparation. It is considerably more toxic than cocaine and should never be used hypodermically. On instillation it produces considerable irritation, smarting and congestion of the conjunctiva. The anesthetic effect is produced more quickly than that of cocaine. There is a slight antiseptic action. Phenacaine does not dilate the pupil, does not cause desiccation of the cornea and does not devitalize the cornea, as cocaine does.

The solution of phenacaine hydrochloride may be sterilized by boiling without its efficacy being affected. A 1 per cent solution has been widely used to produce surface anesthesia for tonometry and the removal of foreign bodies. It has also been employed by some surgeons for intraocular operations, such as extraction of cataract, and with the use of epinephrine to produce ischemia, it is a satisfactory

²³ Sollmann, T. The Comparative Efficiency of Local Anesthetics, *J. A. M. A.* 70:216 (Jan. 26) 1918.

topical anesthetic. However, phenacaine has been pretty generally replaced by butacaine, which, in turn, is now being challenged by tetracaine, because the latter causes little smarting when it is instilled in the conjunctival sac.

Butacaine Butacaine sulfate was introduced in 1920, it is a white, amorphous powder, prepared synthetically by Adams, Kamm and Volwiler. It is freely soluble in water and may be sterilized by boiling without impairment of its efficacy. It does not deteriorate rapidly on exposure to light or air, possibly because it possesses certain antiseptic properties. Butacaine causes precipitation of sodium and other chlorides, so it should not be dissolved in a saline solution.

For instillation butacaine sulfate is generally used in a 2 per cent solution. After a single instillation of a 2 per cent solution, surface anesthesia is usually produced in one minute and lasts from fifteen to thirty minutes. However, two instillations are preferable, an interval of two or three minutes being allowed between each instillation. Patients are not equally susceptible to the action of butacaine, but with two instillations sufficient anesthesia is produced in practically all persons to permit the removal of rather deeply embedded foreign bodies without pain. The depth, degree and duration of the anesthesia are increased by further instillations. Four instillations of a 2 per cent solution of butacaine sulfate at intervals of three minutes produce profound anesthesia of the cornea and conjunctiva, and in five or ten minutes after the last instillation the maximum effect is reached. The average duration of anesthesia is about thirty minutes, but the effect may last as long as an hour. The first instillation causes considerable smarting and irritation and slight hyperemia of the conjunctiva, which may be controlled with epinephrine.

In the literature no toxic symptoms have been reported to follow the topical use of butacaine in the conjunctival sac. The Research Committee of the Council on Pharmacy and Chemistry of the American Medical Association stated that, when injected hypodermically into albino rats, butacaine was two and one-half times as toxic as cocaine.

In the report of the Committee on Local Anesthetics of the Section on Ophthalmology of the American Medical Association,²⁴ butacaine was compared with cocaine as a local anesthetic, and the unanimous opinion expressed by the Committee was that for surface anesthesia butacaine is superior to cocaine, as it acts more quickly and is accompanied by fewer complications. There are no objectionable effects, such as dilatation of the pupil or desiccation of the cornea, and the anesthesia with a 2 per cent solution of butacaine sulfate is more profound than that with a 4 per cent solution of cocaine hydrochloride. Also, no toxic symptoms were noted after the instillation of a 2 per cent solution of butacaine sulfate in the conjunctival sac.

Tetracaine Tetracaine, a derivative of procaine, is one of the newer local anesthetics. For instillation anesthesia its chief advantage over phenacaine and butacaine is the fact that it causes little smarting. It is an odorless, white, crystalline substance, readily soluble in water and fairly stable when exposed to light and air. It may be sterilized by boiling without decomposition and without impairment of its efficacy. According to Wilmer and Paton,²⁵ it is compatible with epinephrine, atropine, homatropine, boric acid, pilocarpine, resorcinol, scopolamine and zinc sulfate.

Various reports agree that when it is given subcutaneously the toxicity of tetracaine is ten times as great as that of procaine, but as it is effective in one-tenth the

24 Bulson, A. E., Jr. Butyn, a New Synthetic Local Anesthetic. Report Concerning the Clinical Use, *J. A. M. A.* 78:343 (Feb. 4) 1922.

25 Wilmer, W. H., and Paton, R. T. *Tr. Am. Ophth. Soc.* 30:31, 1932.

strength of the effective dose of procaine, the relative toxicity is therefore about the same as that of procaine

Schmidt,²⁶ Lundy and Essex,²⁷ Singer,²⁸ and Kiess²⁹ reported on the topical use of tetracaine for infiltration and for spinal anesthesia in over 10,000 cases, representing a great variety of operations. They did not report having observed any toxic effects. Schüleim³⁰ recommended tetracaine because of the prolonged action and the low cost of the drug. He stated that with tetracaine the duration of anesthesia is from four to six hours, whereas with procaine it is only from one and a half to two hours.

Because tetracaine has a powerful hypotonic action in aqueous solution, Wilmer and Paton²⁵ advised the use of isotonic solution of sodium chloride as a solvent. These investigators, in reporting the use of tetracaine in over 500 cases at the Wilmer Ophthalmological Institute, stated that it possesses definite advantages over other local anesthetics.

After two instillations of tetracaine in 0.5 per cent solution, surface anesthesia is produced in about one minute and lasts about twenty minutes. With more instillations at two to three minute intervals deeper and more prolonged anesthesia is obtained. There is some lachrimation, but practically no hyperemia. The corneal epithelium is not disturbed, and the size of the pupil, accommodation and tension are not affected.

When these four local anesthetic agents, cocaine, phenacaine, butacaine and tetracaine, are compared, it will be noted that the chief advantages of tetracaine are as follows:

- 1 Little smarting or congestion of the conjunctiva is produced when the drug is instilled in the eye.
- 2 The action is rapid and prolonged.
- 3 Tetracaine does not dilate the pupil or devitalize the cornea.
- 4 Tetracaine has the same relative toxicity as procaine and therefore a great deal less than cocaine, phenacaine and butacaine.

Occasionally tetracaine may produce conjunctivitis and dermatitis of the lids, similar to that with atropine and other drugs commonly used in the eye. However, this reaction is rarely observed with tetracaine.

Comment. While cocaine is still popular, the chief objections to its use are that it dilates the pupil and may influence the tension. Also, cocaine causes desiccation of the corneal epithelium and tends to devitalize the cornea. The deleterious action of cocaine may retard healing, and in keratoplastic operations it may be responsible for some of the grafts becoming cloudy. It also may account for the more frequent collapse of the cornea observed in cases of cataract extraction. Phenacaine and butacaine have practically no advantages over tetracaine, and they cause more smarting when instilled in the eye. Metycaine, and possibly other local anesthetic agents, may compare favorably with tetracaine, but tetracaine has been found very satisfactory.

Superficial anesthesia sufficient for the removal of foreign bodies from the cornea, tonometry and such minor procedures can be produced in from one to five minutes, the period depending on the anesthetic agent used. Two instillations should be

26 Schmidt, H. *Chirurg* 3 97, 1931.

27 Lundy, I. S. and Essex, H. E. *Proc. Staff Meet., Mayo Clin.* 6 376, 1931.

28 Singer, R. *Wien med. Wchnschr.* 81 1593, 1931.

29 Kiess, T. *Zentralbl. f. Chir.* 57 3090, 1930.

30 Schüleim, M. *München med. Wchnschr.* 78 1475, 1931.

made. The patient is directed to look upward, the lower lid is drawn down, and several drops of the anesthetic are instilled in the lower cul-de-sac. In two or three minutes the second instillation is made. The patient is asked to look downward, the upper lid is raised, and several drops of the anesthetic are allowed to flow under the upper lid and down over the cornea. In this way a more complete anesthesia is produced than if both instillations were given in the lower cul-de-sac.

With two instillations tonometry is less likely to be unpleasant, a point of some importance, since the patient can more easily hold his eye quiet. Also, if the eye is not well anesthetized, the patient may conclude that if this apparently minor procedure is painful, an operation would be unbearable. For deeper anesthesia, four instillations at three minute intervals should be made, and in fifteen minutes the maximum effect is usually produced. To produce ischemia and obtain a bloodless field, as well as to prolong the anesthesia, several drops of epinephrine hydrochloride, 1:1,000, are also instilled.

Regional or Infiltration Anesthesia—Procaine. In selection of the anesthetic for regional or infiltration anesthesia, the first consideration should be that of safety. Second, adequate anesthesia should be produced quickly, without injury or irritation to the tissues, and should be of sufficient duration to allow the surgeon ample time to complete the operation. Third, the anesthetic agent should be easily available, its preparation should be simple, and sterilization by boiling should not cause deterioration.

Procaine fulfils these requirements better than any local anesthetic yet produced. Braun³¹ stated that the toxic action of procaine is less pronounced than that of any hitherto known anesthetic and that it possesses scarcely any irritating properties. Labat³² said "Novocain [procaine] has stood the test for many years and is the drug of choice." The Research Committee of the Council on Pharmacy and Chemistry of the American Medical Association reported that procaine is the least toxic local anesthetic. The Committee on Local Anesthetics in Ophthalmic Work of the American Medical Association^{32a} recommended it as the most desirable drug for infiltration anesthesia. Procaine is now so generally accepted as the safest and best agent for production of all regional and infiltration anesthesia that a consideration of other more toxic and less satisfactory drugs seems unnecessary.

The salt (hydrochloride) of procaine crystallizes from alcohol in the form of needles, which melt at a temperature of 156°C. It is soluble in equal quantities of water, producing a solution which is neutral in reaction and readily soluble in isotonic solution of sodium chloride. It is precipitated by alkaline reagents, such as sodium carbonate, to form an insoluble base. The crystals may be sterilized in the autoclave at a temperature of 110°C, and the watery solution may be sterilized without deterioration by boiling. Procaine is rapidly and completely absorbed locally, with no destruction of the tissues. As there is no peripheral effect on the blood vessels, the anesthetic effect is of short duration, so that it is necessary to use epinephrine to prevent the rapid absorption of the drug. With the addition of a small amount of epinephrine to the procaine, analgesia begins almost immediately after the injection and lasts two to three hours. Surgical anesthesia starts ordinarily in from five to ten minutes and continues one and one-half to two hours.

Procaine is not so well suited to production of anesthesia of mucous membranes by topical application probably owing to the fact that it does not completely penetrate these membranes.

³¹ Braun,⁴ p. 117.

³² Labat,²² p. 40.

^{32a} Report of Committee on Local Anesthetics in Ophthalmic Work of the American Medical Association, Trans. Sect. Ophthalm. A. M. A., 1921, p. 308.

Braun³³ stated that a 0.4 per cent solution of potassium sulfate added to the solution of procaine hydrochloride greatly increases its anesthetic properties and in this concentration produces neither local nor general injury. When procaine is used in weak solutions and in doses sufficient to produce surgical anesthesia, its toxicity is negligible. Labat³⁴ gave the maximum dose of procaine hydrochloride for robust patients in good physical condition as 150 cc of a 1 per cent solution and 60 cc of a 2 per cent solution and emphasized the importance of the proper technic and of slow injection.

Although toxic symptoms are rarely encountered in ophthalmic operations, in which small quantities of the drug are used, a small amount of a 1 or 2 per cent solution injected rapidly or directly into the circulation may produce toxic symptoms. These symptoms are rapid pulse, palpitation, frequent, labored breathing, pallor of the face, cyanosis of the fingers, lips and ears, nausea, vomiting, cold sweats, and blurred vision. The rapid pulse, palpitation and rapid and labored breathing may also be due to epinephrine, are of short duration, lasting two to three minutes, and are not serious. If they do occur, the injection should be stopped, in the event of more serious symptoms, such as pallor, cyanosis and nausea, Labat³⁵ recommended subcutaneous injection of the following cardiac stimulant: caffeine, 0.25 Gm, sparteine sulfate, 0.05 Gm, sodium benzoate, 0.30 Gm, and strychnine sulfate, 0.001 Gm, put up in a 2 cc ampule. After the patient has completely recovered, the injection of the procaine may be resumed.

It is important to prepare an isotonic solution, as hypertonic solutions cause shrinkage, and hypotonic solutions swelling, of the cells, with either, destruction of the tissue occurs. Isotonic solution of sodium chloride is consequently the solvent of choice.

Labat³⁶ emphasized the importance of the use of only freshly prepared solutions and of the addition, just before use, of 5 drops of colorless epinephrine hydrochloride, 1:1,000, to 100 cc of the anesthetic solution, irrespective of the strength of the solution. Until 1920 Labat used 20 drops of epinephrine hydrochloride, 1:1,000, to every 100 cc of the solution of procaine hydrochloride, but he gradually reduced the quantity to 5 drops and observed that toxic symptoms were less frequent and the reactions not so pronounced. Solutions of epinephrine that have become brown or pink should be discarded.

For the average patient the maximum dose of epinephrine hydrochloride, 1:1,000, given subcutaneously or intramuscularly is 10 minims (0.62 cc). For elderly patients—those with arteriosclerosis and other lesions of the vascular system or diabetes—who are frequently encountered in ophthalmic practice, the amount should be reduced to 5 drops.

As the quantity of anesthetic solution used in ophthalmic operations is so small—rarely more than 10 cc—one need be concerned little about exceeding the maximum safe dose of epinephrine if the proportion of 5 or 10 drops of the 1:1,000 dilution of epinephrine hydrochloride to 100 cc of anesthetic solution is observed. The advantages usually ascribed to the addition of epinephrine to the procaine solution are that it hastens, intensifies and lengthens the anesthetic action of the procaine.

For minor operations that are performed in the office or the hospital, often requiring less than 1 cc of 2 per cent procaine hydrochloride, a convenient and economical preparation is offered by several pharmaceutical houses. The procaine

33 Braun,⁴ p 119

34 Labat,²² p 41

35 Labat,²² p 45

36 Labat,²² p 46

and epinephrine are furnished in ampules containing 1 cc of a 2 per cent solution of procaine hydrochloride with epinephrine hydrochloride 1 50,000 or 1 20,000 in concentration, sterile and ready for use. Larger ampules can also be procured, so that for the ophthalmic surgeon whose operations are somewhat scattered the use of such ampules, in which the dose is accurate and the percentage assured, is a decided advantage for both office and hospital work.

INSTRUMENTS

Syringes—The Luer-Lok 2 and 5 cc syringes (fig 1) have been found satisfactory. These syringes have a lock which prevents the needle from coming off during the injection. They are lighter than the Labat syringes, which were formerly used, and are shown in figure 1. The Luer-Lok syringe is not damaged by being placed in a boiling sterilizer.

Needles—Three sizes of needles are desirable: a 27 gage needle, 12.5 mm in length, for subconjunctival injections, production of intradermal wheals and small subcutaneous injections; a 25 gage needle, 2 cm in length, for deeper subcutaneous injections, production of akinesia, etc.; and a 22 gage needle, 3.5 cm long, for still deeper injections, such as retrobulbar injection within the muscular cone and blocking of the lid. Platinum-iridium needles seem to pass through the skin and tissues a little easier than steel needles. However, the rustless steel needles are satisfactory. The protective metal shield or holder for the needle prevents the point from becoming dulled or turned.

NERVE BLOCK, FIELD BLOCK AND INFILTRATION ANESTHESIA

Intradermal Wheal (fig 2)—Before the skin is pierced for an injection, an intradermal wheal should be made to avoid production of unnecessary pain. For this purpose the 27 gage needle is used. The skin is stretched with the index finger, and the needle is held flat against the skin. The point of the needle is then introduced just under the epidermis, with the bevel edge up, and a little procaine-epinephrine solution is injected; this gives the site of the injection a somewhat bleached appearance, and the skin immediately becomes insensitive. For the skin of the lids, which is extremely thin and loose, a little fold may be made with the thumb and the index finger, the needle inserted at the summit of the fold and a similar wheal raised.

Local Anesthesia—By this term, one usually refers to a procedure by which a part of the body is rendered insensitive to pain, whether by topical application of the anesthetic agent, infiltration at the site of the incision or regional anesthesia, which Labat³⁷ defined as "the result of a certain number of delicate surgical procedures by which it is possible to control pain temporarily by interrupting the sensory nerve conductivity of any region of the body. Motor function is occasionally interfered with."

Local anesthesia may be produced in two ways:

- 1 By nerve block, which is accomplished by injection of the anesthetic agent around the nerve supplying the part, so that the conductivity of the nerve is interfered with.

- 2 By field block, in which a wall of anesthesia is produced that renders the operative field insensitive to pain. This wall of anesthesia blocks all the nerves supplying the operative field and does not aim at any individual nerve, as in nerve block. First, an intradermal wheal is raised, through which the needle is introduced

³⁷ Labat,²² p. 1

perpendicularly, the solution is injected slowly as the needle advances until it reaches the deepest layers of the soft tissues into which injection is to be made. The needle is then withdrawn until the point reaches the subcutaneous tissues, and the solution is slowly injected as the needle is withdrawn. The direction of the needle is then changed, the point being advanced along the line to be blocked and the needle introduced obliquely. This procedure is repeated several times, the needle being inclined more obliquely each time. A second wheal is then raised in line with the first, and the procedure is repeated until a wall of sufficient length is produced. It is often necessary to surround the operative area with a wall of anesthesia, the width depending on the nerve supply of the part to be operated on. This procedure is applicable in some plastic operations, and the principal advantage is the lack of infiltration of the operative field, which might interfere with healing or distort the tissues of the part involved. Also, if there is much scar tissue, the field cannot be infiltrated satisfactorily. With field block the anesthesia lasts longer because the anesthetic solution does not escape when the incision is made, as it does when the tissue along the site of the incision is infiltrated.

In production of regional anesthesia it is extremely important to visualize the anatomic features of the operative field, particularly with regard to the nerve

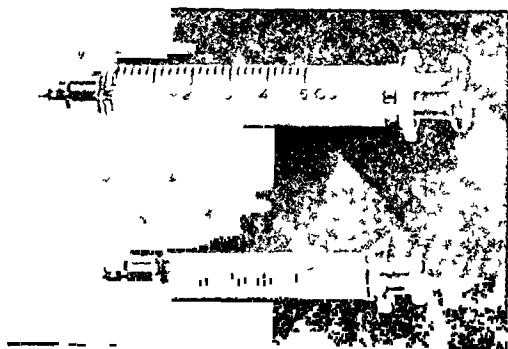


Figure 1

Fig 1—Lucr-Lok syringes, of 2 and 5 cc capacity

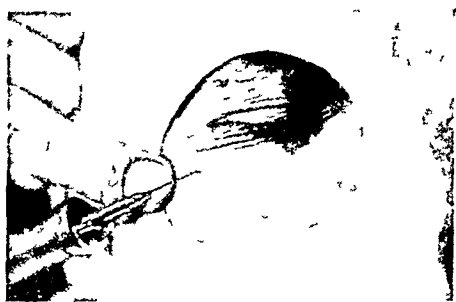


Figure 2

Fig 2—Technic of production of intradermal wheal

distribution and the bony landmarks that serve as a guide for the various injections. It is assumed that an accurate knowledge of the anatomic relations has been acquired and the only references to the structure involved will be in connection with the technic employed.

Anesthetic Solution—The anesthetic solution used in production of the following forms of anesthesia, unless otherwise stated, contains procaine hydrochloride, 2 per cent, and epinephrine hydrochloride 1:1,000, 1 drop to each 5 cc of anesthetic solution being used.

Infiltration Anesthesia—After an intradermal wheal is raised, the needle is introduced through the wheal and the anesthetic solution is injected slowly as the needle advances. If there are any large vessels in the vicinity, one should aspirate the contents of the needle occasionally to make sure that the needle has not entered a vessel.

Subconjunctival Injection—For this procedure the 2 cc syringe with the 27 gage needle is used. The lids are held open with the thumb and finger or with a speculum. The point of the needle is slid gently over the conjunctiva until a fold appears in front of the point; the syringe is then rotated a boring effect being

produced. In this way even a dull needle passes easily and gently through the conjunctiva without the necessity of forceps or of quick jabbing.

Many excellent articles dealing with anesthesia in ophthalmic surgery have been published, but often specific and minute details regarding the technic have been omitted, the authors evidently assuming that their readers were familiar with them. From personal observation, this assumption seems hardly justified, it is with some temerity, however, that space is given to these important, although familiar, academic details.

RETROBULBAR INJECTION WITHIN THE MUSCULAR CONE

Indications—Indications for this procedure are (1) enucleation and evisceration, (2) intraocular operations, and (3) operations in which there is considerable traction on the muscles, such as advancement of an extraocular muscle.

Procedure and Comment—The retrobulbar injection should be preceded by production of the usual instillation anesthesia. A small intradermal wheal is first raised a short distance below the inferior temporal margin of the orbit (fig. 2).



Figure 3



Figure 4

Fig. 3—Skull, showing position of the needle for retrobulbar injection within the muscular cone.

Fig. 4—Retrobulbar injection within the muscular cone (Atkinson, W. S. Local Anesthesia in Ophthalmology, Tr. Am. Ophth. Soc. 32:399, 1934).

When injection is to be made into the right orbit, the patient is directed to look upward and to the left (figs. 3, 4 and 5). The 22 gage needle, 3.5 cm. in length, is then introduced through the wheal, and the skin is moved upward with the needle so that the point just clears the inferior orbital margin. The needle is then directed upward and inward, midway between the external and the inferior rectus muscles, and is advanced toward the apex of the orbit for 2.5 to 3.5 cm., the distance depending on the size of the orbit. When the needle has reached a depth of from 2.5 to 3.5 cm., one should aspirate the contents before the solution is injected in order to be sure that the needle has not entered a vessel. However, in this location it is practically impossible to enter a vessel unless it is anomalous, since the vessels here are normally smaller than the needle and are freely movable. From 1 to 1.5 cc. of the 2 per cent solution of procaine hydrochloride is injected slowly, care being taken not to produce undue proptosis by too large an injection. For the majority of operations on the globe 1 cc. is sufficient but for some operations on

muscles and for enucleation 3 cc or more may be injected, as the ptosis does no harm and, particularly with painful eyes, more procaine is desirable

Gentle massage with a rotary motion of the globe causes the procaine solution to become more thoroughly diffused within the muscular cone. In this way more complete and rapid anesthesia is produced. Anesthesia of the muscles is not obtained as rapidly as anesthesia of the globe, so for enucleation and operations in which there is considerable traction on the muscles it is advisable to wait five or ten minutes before beginning the operation.

By means of the injection within the muscular cone, all of the sensory nerves to the eyeball are blocked, and complete anesthesia of the globe is obtained regardless of how inflamed or painful the eye may be. Pressure on the inflamed eye, which before the injection caused severe pain, is not noticed now. The rectus muscles, except the superior rectus, are also rendered practically insensitive to traction.

The injection within the muscular cone also causes paresis of the rectus muscles except the superior rectus, so that the patient cannot easily look down. There-

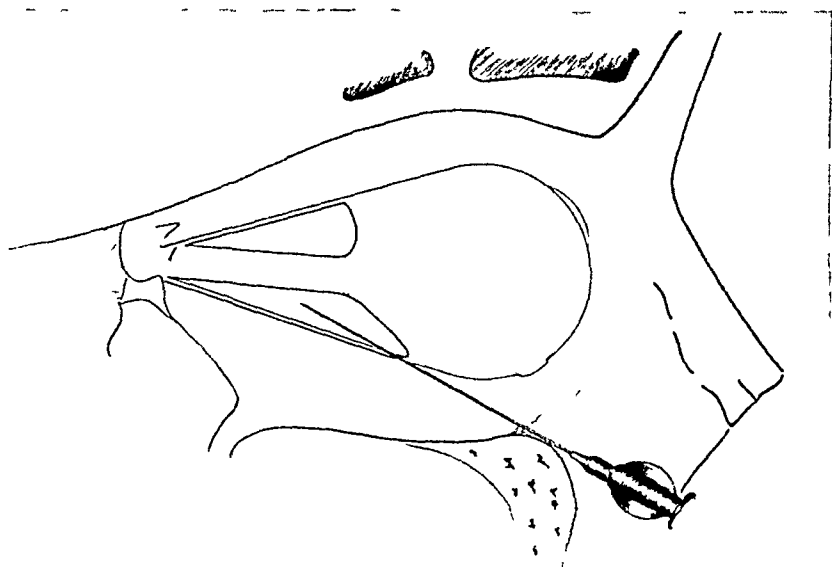


Fig 5—Diagrammatic sketch showing the eye turned up and away from the site of the injection, so that the fascial extension is moved forward and up, out of the way

fore, for such operations as extraction of cataract it is advisable to use a suture under the superior rectus muscle (bridle suture), but with the rectus muscles inactive little traction is required to hold the eye in the desired position and better fixation of the globe is thus obtained. Also, with paresis of the rectus muscles the so-called squeeze, with loss of vitreous, caused by their contraction is less likely to occur.

The superior rectus muscle usually remains active and may be sensitive to traction. For prevention of pain when this muscle is picked up for the introduction of a bridle suture or for an operation in which there is traction on the muscle, additional anesthesia is necessary. This may be accomplished by an injection of 0.5 cc of the anesthetic solution through the conjunctiva of the upper cul-de-sac. With the superior rectus muscle active and with paresis of the other extrinsic muscles, there is torsion of the globe, with rotation toward the nose. The torsion is increased when a suture is used under the superior rectus muscle. Therefore, if iridectomy is to be performed, it should be done from 10 to 15 degrees to the nasal

side, so that the coloboma will be at axis 90 when the muscles again function normally. While this is of no particular importance from a visual standpoint, a coloboma looks better in the vertical meridian.

When the eye is red and inflamed, as in cases of acute glaucoma, a subconjunctival injection should also be given, since the inflamed conjunctiva is not well anesthetized by topical application. Only the conjunctiva immediately surrounding the cornea for a distance of about 3 or 4 mm is rendered insensitive by an injection within the muscular cone, since its nerve supply is from the ciliary nerves, which are within the cone. The rest of the conjunctiva is innervated by the supraorbital, supratrochlear, infratrochlear, infraorbital and lacrimal nerves, all of which are outside the muscular cone and are seldom reached by the anesthetic injected within the cone. When the eye is inflamed, less pain is caused if the subconjunctival injection is given after the retrobulbar injection. For the subconjunctival injection the

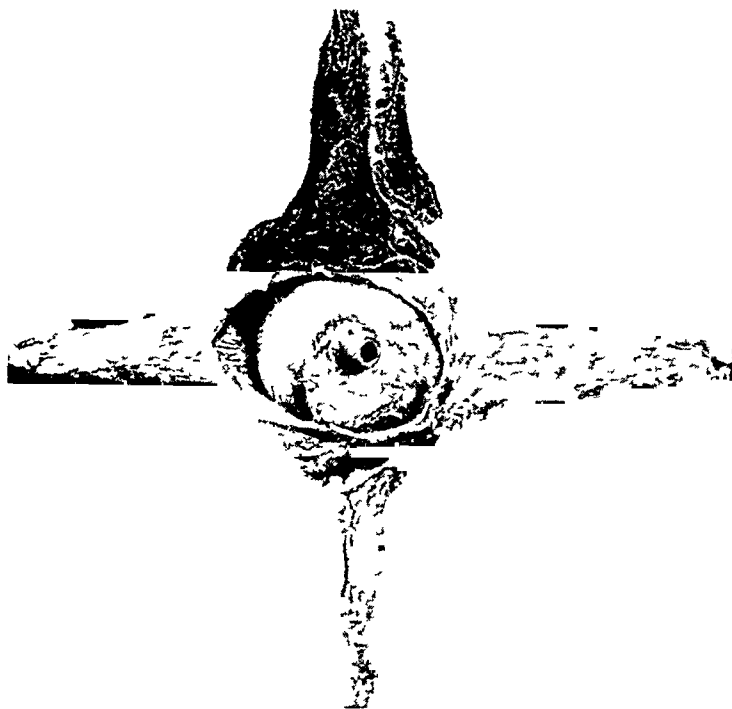


Fig 6—Posterior view of the eyeball, showing the fascial sheaths and, in part, the fascial extension which closes the spaces for a little distance back of the globe (from Whitnall³⁸)

needle may be introduced through the insensitive conjunctiva directly surrounding the cornea, and if succeeding injections are made through blebs produced by the anesthetic, little pain will be experienced. In this way, pain due to the use of fixation forceps and to suture of the conjunctiva is avoided in eyes that are inflamed and painful.

With such complete anesthesia of the globe, and the eye practically immobile, together with paralysis of the orbicularis muscle, operations on the globe can be performed with the same deliberate precision that one can use when operating on a pig's eye.

If the patient looks upward and away from the site of the injection, access to the muscular cone is easier. The extension of the fascial sheath of the muscles which closes the spaces between the rectus muscles for a little distance back of the globe is in this way moved forward and upward, out of the way, so that the needle does not strike it, as is shown diagrammatically in figure 5. If the needle does strike the sheath, pain is produced. The sheath is also somewhat tough, and the needle

does not penetrate it easily, with the result that the globe rotates, which to some extent interferes with the introduction of the needle and the equilibrium of the patient

Procaine injected within the muscular cone is apparently held within the cone, since the nerves outside the muscular cone are rarely affected. How is the solution of procaine held within the muscular cone, since there is no demonstrable fascia between the rectus muscles, posterior to the globe, as they converge to their attachment at the apex of the orbit? Anteriorly, the escape of fluid is prevented by the globe, surrounded by Tenon's capsule, and by the adjacent margins of the sheaths of the four rectus muscles, which are continuous with one another, with a wide sweep between them, as shown in figure 6 (from Whitnall,³⁸ fig 15). In this manner, an intramuscular membrane is formed which, according to Whitnall, exists for a short distance behind the globe. Beyond this the muscles converge to their attachment through the annulus of Zinn, at the apex of the orbit, and their margins come closer together, so that comparatively little space is left between them. In this

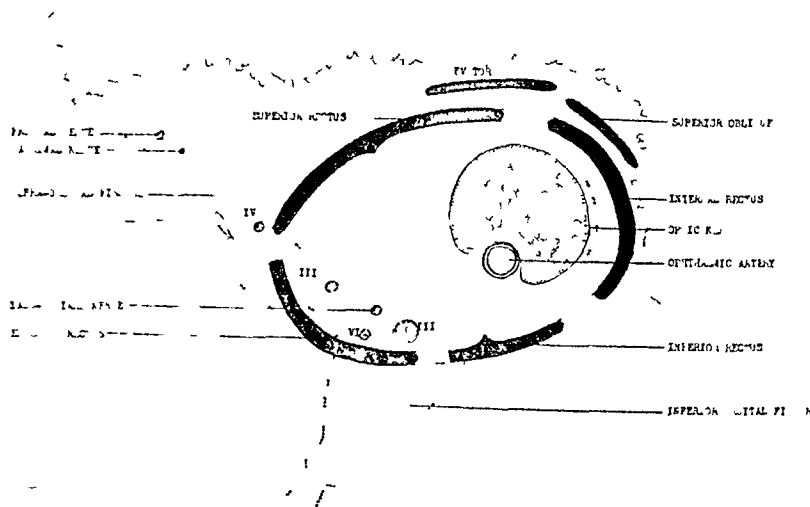


Fig 7—Scheme showing the position of the annulus of Zinn and the relative position of the nerves which enter the orbit through the superior orbital fissure, both within and outside the annulus (after Whitnall³⁸ and Poirier [*Traite d'anatomie humaine*, ed 3, Paris, Masson & Cie, 1911, vol 5])

location the escape of the procaine solution is probably prevented, or at least retarded, by the closely packed layer of fat, with its connective tissue reticulum.

According to Whitnall,³⁹ the orbital fat which fills the entire space in the orbit not occupied by other structures varies in consistency in different regions. Within the muscular cone the fat has the appearance of large and loosely connected lobules, broken up by the passage of the nerves and vessels. Outside the muscular cone the fat is more firmly and closely packed and contains a quantity of connective tissue, which is closely attached to the muscular sheaths. No doubt this fat and connective tissue serves as a sufficient barrier so that the anesthetic solution is held within the cone with production of anesthesia or blocking of the nerves that traverse it, namely the nasociliary nerve, the long and short ciliary nerves, the ciliary ganglion, the optic nerve and all the motor cranial nerves except the trochlear, or fourth (figs 7 and 8).

³⁸ Whitnall, S. E. *The Anatomy of the Human Orbit and Accessory Organs of Vision*. London, H. Frowde, Hodder & Stoughton, 1921.

³⁹ Whitnall³⁸ p. 297.

A decrease in the intraocular tension occurs after injection within the cone. If the amount of epinephrine hydrochloride (1:1,000) is increased to 3 drops to 5 cc of the anesthetic solution, the decrease in the intraocular tension is greater, and a decrease of as much as 20 to 30 mm of mercury may be noted in cases of acute glaucoma with high tension.

After the injection within the cone there is often noticeable deepening of the anterior chamber, particularly when the amount of epinephrine hydrochloride is increased. This indicates a decrease in the fluid contents of the eye posterior to the diaphragm. The incision is thus made easier in cases in which the chamber has been shallow. Also, with lowering of the pressure behind the lens the anterior capsule appears to become relaxed. In some cases the capsule of the lens, which prior to operation appeared to be too tight to be grasped with smooth forceps, was found to be loose after an injection within the cone, so that a good bite of the capsule could be obtained with the forceps.

With some methods of intracapsular extraction of cataract a decrease in the intraocular tension seems to be an advantage, as it lessens the possibility of prolapse

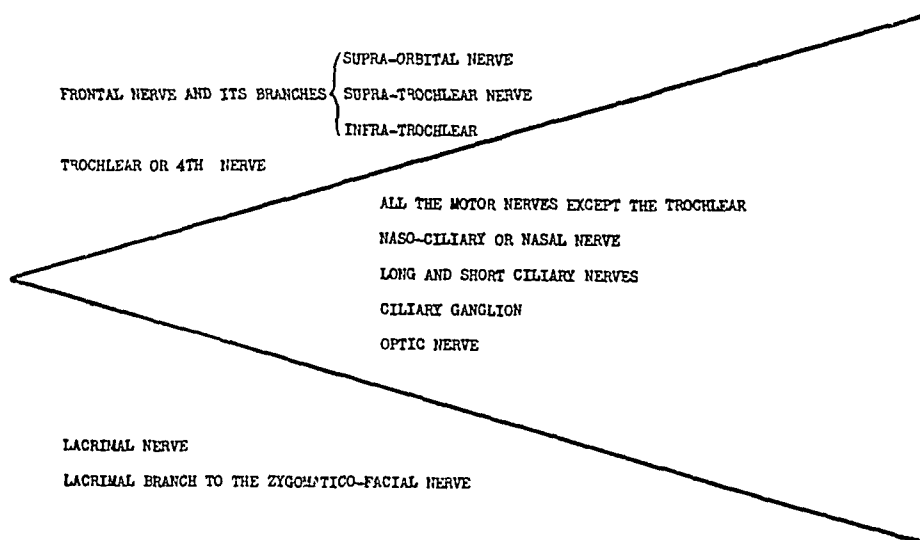


Fig 8—Diagram of nerves within and outside the muscular cone

of the vitreous. In extraction with capsulotomy it is often more difficult to express the lens when the tension is decreased. With deeply set eyes the operation is somewhat facilitated if the eye is slightly proptosed. With lowered tension the iris may not prolapse well in corneoscleral trephining, an incident which may be embarrassing. The decrease in the intraocular tension following the injection of procaine and epinephrine within the cone may be accounted for by the constricting action of the epinephrine on the arteries entering the globe, an effect which would tend to decrease the amount of blood entering the globe but would not impede its exit through the venae vorticosae, since the solution does not reach them, located as they are in the episcleral space. The free anastomosis of the venae vorticosae and other orbital veins with the facial vein allows free exit of the blood.

Newly formed aqueous which Duke-Elder⁴⁰ termed "plasmoid aqueous," contains a larger proportion of colloid molecules, or plasma proteins, than does the normal aqueous. If this fluid is a dialysate due to dilatation of the capillaries of the ciliary body after escape of the normal aqueous, then injection of procaine and epinephrine within the cone not only would be of value as an anesthetic but, as

⁴⁰ Duke-Elder, W. S. The Nature of the Intra-Ocular Fluids, British Journal of Ophthalmology, Monograph Supplement 3, London, George Pulman and Sons, 1927.

pointed out by Friedenwald,⁴¹ would prevent a postoperative increase in tension. The action of the epinephrine reduces the edema of the intraocular tissue, particularly that of the ciliary body and ciliary processes. Thus, dialysis is limited, and more nearly normal aqueous is formed, which diminishes the occurrence of so-called plastic iritis and the formation of synechiae.

This simple and efficient method of obtaining complete anesthesia of the globe has been revived, in a great measure, by the investigations of Lowenstein,¹² under the direction of Elschnig. With a view to injection into the ciliary ganglion for complete anesthesia of inflamed and painful eyes for enucleation, Lowenstein made a study of the exact location of this ganglion. By using a 5 cm. needle and introducing it through the conjunctiva temporally, just below the margin of the external rectus muscle, for a distance of 4.5 cm., he found the point to be just in front of the ganglion. Injections made in this manner within a few minutes produced complete insensibility of the most painful eyes.

Later, Elschnig modified the technic and introduced the needle through the skin at the inferior temporal margin of the orbit, rather than through the conjunctiva. The suffering caused by traction and pressure on painful eyes is thus avoided. The method also allows easier access to the muscular cone. In observations on the cadaver, Lowenstein noted that the optic nerve was often pierced with a 5 cm. needle and that a dye could be injected into the optic sheath readily without any dye's being found free in the orbit. This indicates how easily the optic nerve may be injured if a 4.5 or a 5 cm. needle is used. The procedure of Lowenstein has been referred to as injection into the ciliary ganglion. It is not surprising that many surgeons have hesitated to try it, and well they might, if the term is taken literally. It would, indeed, require the most exact technic to inject an anesthetic into the tiny, elongated ganglion, 2 mm. in length, lying as it does in the orbital fat within the muscular cone, about 1 cm. in front of the annulus of Zinn, between the external rectus muscle and the optic nerve, and close to the ophthalmic artery. That it is desirable to block the ciliary ganglion for many operative procedures is not questioned. But this can be done safely and easily by use of a 3.5 cm. needle and injection of the anesthetic solution more anteriorly within the muscular cone. In this location, because of the loosely connected fat lobules, the solution diffuses quickly and permeates thoroughly the ciliary ganglion, a fact undoubtedly appreciated by Knapp¹⁰ nearly fifty years ago, when he employed and reported on the use of retrobulbar injection to produce anesthesia of the globe for enucleation.

Duverger,⁴² after experiments on the cadaver with needles of various lengths concluded that a 3.5 cm. needle is preferable for all orbital injections except those to be made at the extreme apex, and for these he found that the 4.5 cm. needle was just long enough to reach the optic foramen, but not to pass through it. With the 3.5 cm. needle Duverger was unable to pierce the optic nerve even after he had removed the temporal portion of the orbital wall so that he could observe the point of the needle, which had been introduced at the inferior temporal margin of the orbit. The point of the needle always eluded the nerve, because in this location the nerve is freely movable. The same property applies to the vessels here. They, also, are small, so that the risk of one's injuring them is slight. Nevertheless, the possibility of orbital hemorrhage is often mentioned as an objection to retrobulbar injection. Data on over 8,000 retrobulbar injections showed 8 orbital hemorrhages, 5 of which were admittedly due to faulty technic. In no instance was the eye damaged. If a

⁴¹ Friedenwald, I. S. *Am J Ophth* 15:189, 1932.

⁴² Duverger, C. *L'anesthésie locale en ophtalmologie*, Paris, Masson & Cie, 1920.

4 5 or 5 cm needle is used and the point is carried to the apex of the orbit, obviously a vessel or the optic nerve might easily be pierced, because here they converge to reach their bony exits and are fixed This danger is avoided by the use of a 3 5 cm needle Duverger also claimed that the best approach for injection within the muscular cone is from the inferior temporal margin of the orbit

Branches and Sensory Distribution of the Ophthalmic and Maxillary Divisions of the Trigeminal Nerve

Nerve	Branches	Ophthalmic Division	Sensory Supply
Frontal	{ Supraorbital Supratrochlear	{ Internal frontal External frontal Branch to infratrochlear	{ Eyelids Diploe and frontal sinus Skin of forehead above head of eyebrow Skin and conjunctiva of upper lid and side of nose
		{ Sensory root to ciliary ganglion Two long ciliary nerves	{ Eyeball Cornea Iris Ciliary body Bulbar conjunctiva immediately around cornea Sheath of optic nerve
Nasociliary	{ Infratrochlear, or external nasal	{ Internal canthus Skin and conjunctiva mainly of upper lid, some of lower lid Root of nose Lacrimal sac Canaliculi Caruncle	
		{ Internal nasal	{ Mucous membrane and anterior part of septum Middle and inferior conchae Lateral wall of nose Skin and cartilaginous end of nose
Lacrimal	{ Anastomosis with the zygomaticotemporal branch of zygomatic	{ Lacrimal gland Conjunctiva and skin of upper lid temporally	
		{ Skin of forepart of forehead up to lateral side of orbit Skin of cheek	
Maxillary, or Second, Division			
Recurrent, or middle meningeal			{ Dura mater
Zygomatic	{ Temporal—communicates with lacrimal nerve Malar	{	{ Skin of forepart of forehead up to lateral side of orbit Skin of cheek
			{ Palate and nasal cavity Periorbital Orbitalis muscle (involuntary)
Sphenopalatine	{	{	{ Sphenoid sinus Posterior ethmoid cells
			{ Minute fibers to
Posterior superior alveolar			{ Molar teeth Gums
Middle superior alveolar			{ Mucous membrane of maxillary sinus Two premolar teeth
Anterior superior alveolar	{	{	{ Lower part of lacrimal sac and nasal duct Mucous membrane of nasal cavity Incisor and canine teeth
			{ Skin and conjunctiva of lower lid Skin of side of nose
Infraorbital	{ Inferior palpebral External nasal	{	{ Skin of cheek Mucous membrane and skin of upper lip
			{ Superior labial

Elschnig, in a personal communication, on Nov 18, 1930, stated that he had made orbital injections regularly for more than five years In about 2,000 intra-bulbar operations, 4 orbital hemorrhages occurred, which Elschnig attributed to faulty technic They did no harm, although in 1 case the operation had to be postponed until the following day

The table shows at a glance the branches and the sensory distribution of the ophthalmic and the maxillary, or second, division of the trigeminal nerve

OPERATION ON THE LACRIMAL SAC

Anesthesia for operation on the lacrimal sac is obtained by blocking the external nasal, or infratrochlear, and the infraorbital nerve

The infratrochlear nerve is the direct continuation in the orbit of the nasociliary, or nasal, nerve after the larger branch leaves the orbit by passing through the anterior ethmoid foramen (fig 9) The infratrochlear nerve lies close to the superior nasal wall of the orbit It runs beneath the superior oblique muscle and the trochlea, and at this point there is a communicating branch to the supratrochlear nerve Before piercing the septum orbitale the infratrochlear nerve divides into several branches to supply the skin and the conjunctiva of the lids near the internal canthus the canaliculi the caruncle the lacrimal sac and the root of the nose

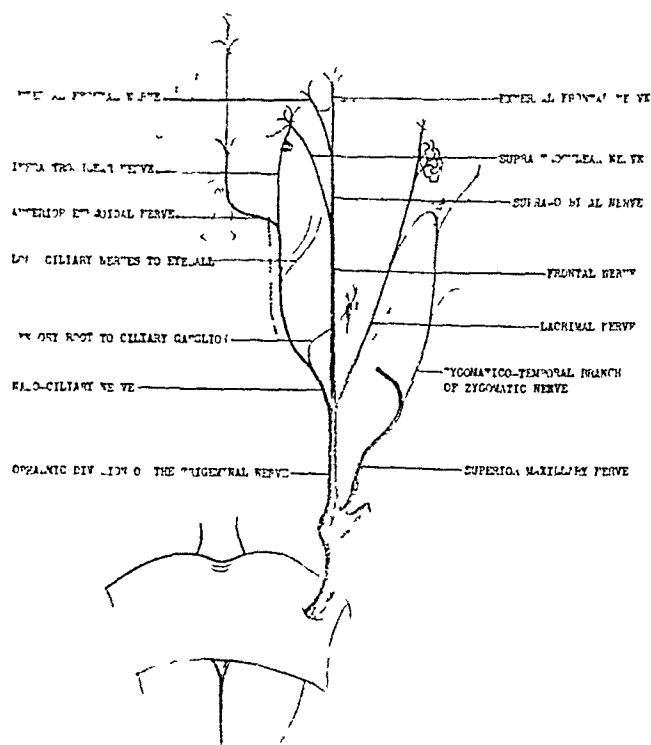


Fig 9—Diagram showing the distribution of branches of the ophthalmic division of the trigeminal nerve (after Whitnall, p 342³⁵)

BLOCK OF THE INFRATROCHLEAR NERVE

A wheal is raised at the superior nasal angle of the orbit A 3.5 cm needle is then introduced through the wheal just a little above and to the nasal side of the trochlea (figs 11 and 12) It should be kept close to the superior nasal wall, and a small quantity of procaine solution should be injected as the needle advances At a depth of about 3 cm 2 or 3 cc of a 2 per cent solution of procaine hydrochloride with epinephrine hydrochloride is injected On withdrawal of the needle, about 0.5 cc should be injected along the orbital margin in the vicinity of the supraorbital notch anterior to the septum orbitale but close to the periosteum Occasionally the angular vein is pierced but if care is taken not to inject the solution while the needle is in the lumen no harm will be done although the resulting ecchymosis is annoying

BLOCK OF THE INFRAORBITAL NERVE

Anatomic Relations—The superior maxillary nerve enters the orbit through the inferior orbital fissure at about its midpoint and is then called the infraorbital nerve. The infraorbital nerve runs forward along the floor of the orbit, beneath the periorbita, in the infraorbital groove and canal. In the forepart of the infraorbital canal, a few millimeters from the foramen, the anterior superior alveolar branch is given off. This small branch passes through minute osseous canals to supply the lower part of the lacrimal sac and the nasal duct, as well as the incisor and the canine teeth. The infraorbital nerve passes through the infraorbital foramen and divides



Fig. 10—Approximate positions of the main vessels of the face which should be avoided, particularly in blocking the infratrochlear nerve (from Whitnall³⁸)



Figure 11

Fig. 11—Skull, showing needle in position to produce block of the infratrochlear nerve



Figure 12

Fig. 12—Method of blocking the infratrochlear nerve

into its terminal branches to supply the conjunctiva and skin of the lower lid, the skin of the cheek, the skin of the side of the nose and the skin and mucous membrane of the upper lip.

The infraorbital foramen is located about 0.5 to 1 cm. below the inferior orbital margin, about 2.5 cm. from the midline of the face, and in line with the supraorbital notch. Just below the center of the inferior orbital margin a depression can usually be felt in which the foramen is located.

The infraorbital canal is from 1 to 1.5 cm in length, and the angle varies considerably in different skulls. A grooved depression leads up to the foramen and aids considerably in location of the latter. After the needle enters the foramen, the angle of the needle can be changed to correspond to the angle of the canal, and the needle can then be introduced easily, with practically no resistance.

Procedure—A wheal is raised about 1 cm from the middle of the ala of the nose. The same needle is introduced through the wheal almost to the bone and is then directed upward and temporally at an angle of about 20 degrees (figs 13 and 14). As the needle advances the procaine solution is injected. The point of the needle is kept in contact with the bone until the foramen is felt, it is then introduced from 0.5 to 1 cm along the infraorbital canal and 1 cc of a 2 per cent solution of procaine hydrochloride is injected. The needle should be introduced into the canal, otherwise the anterior superior alveolar nerve will not be blocked. If this nerve is not blocked, some pain may be experienced when the sac is excised at the entrance of the nasal duct and when the nasal duct is curetted.

Labat⁴³ suggested that the left index finger be placed over the foramen, as an indication of its location and the axis of the infraorbital canal. This makes it easier



Figure 13



Figure 14

Fig 13—Skull showing the needle in position for injection into the infraorbital canal to block the infraorbital and the anterior superior alveolar nerve. (A 3.5 cm needle was used in this picture in order better to show the angle, but for the injection the 2 cm needle is used.)

Fig 14—Injection into the infraorbital canal to block the infraorbital and anterior superior alveolar nerves.

to find the foramen with the needle. Injection into this nerve produces anesthesia of the conjunctiva and the skin of the lower lid, the skin of the cheek, the skin of the side of the nose, the skin and the mucous membrane of the upper lip, the lower part of the lacrimal sac, the nasal duct and the incisor and canine teeth.

For the operation of dacryocystorhinostomy, besides block of the infratrochlear and the infraorbital nerve, topical anesthesia of the nasal mucous membrane should be obtained by the use of a nasal pack.

FIELD BLOCK FOR ANESTHESIA OF THE LIDS

Since there are so much overlapping and variation in the sensory nerve supply of the lids (fig 15), it is simpler in operations involving a considerable area of the lids to produce a field block rather than to try to block the individual nerves.

⁴³ Labat,²² p 117

Procedure—A wheal is raised at the center of the orbital margin (fig 15), above or below, the position depending on which lid is to be blocked, and the 35 cm needle is introduced through the wheal. The point of the needle should follow the orbital margin closely but should not penetrate the orbital septum. A 2 per cent solution of procaine hydrochloride with epinephrine hydrochloride (1:1,000) is injected slowly as the needle advances. In order to inject the anesthetic all along the margin and to infiltrate well the tissue around the nerves that emerge from the orbit, it is necessary to withdraw the needle a little and redirect it several times. The injection should not be made just under the skin, but should be done close to the periosteum. About 0.5 cc of the anesthetic solution should be injected deep in the vicinity of the supraorbital notch.

After the anesthetic solution has been injected along one-half the superior or the inferior orbital margin, the location depending on which lid is to be blocked,



Fig 15—Right eye. The sensory nerve supply is shown by solid lines and the orbital margin by the dotted outline. Left eye. The dot and arrows indicate the site and direction of the injection (modified from Whitnall, pp 20 and 176³⁸).

the needle is partially withdrawn, it is then redirected and the solution injected along the other half of the orbital margin.

For removal of small tumors of the lids, such as papilloma, infiltration at the site of the tumor is usually sufficient and is the simplest method. It also decreases the bleeding. For chalazion and operations involving the margin of the lid, which, owing to its rich nerve supply, is extremely sensitive, instillation anesthesia and infiltration at the site of the chalazion are often not sufficient to make the operation painless. However, instillation anesthesia and an injection of 1 cc of the anesthetic solution through the conjunctiva of the cul-de-sac in the area corresponding to the chalazion more frequently produce complete anesthesia.

In operations in which large conjunctival flaps are raised, instillation anesthesia is often not sufficient and pain may be experienced, particularly when the flap is

sutured. This may be due to the incomplete anesthetization of the deeper layers of the conjunctiva or the subconjunctival tissue or to the rapid escape of the tissue fluids when the flap is raised, which favors the more rapid return of sensibility. This is also true in operations for pterygium. By the use of subconjunctival injections in such operations unnecessary pain is avoided.

AKINESIA

The desirability of production of temporary paralysis of the orbicularis muscle by block of the temporofacial division of the facial nerve for intraocular operations, particularly extraction of cataract, is so generally conceded that comment is unneces-



Fig 16—Method of block of the temporofacial division of the facial nerve to produce temporary paralysis of the orbicularis muscle

sary. Of the various modifications of the van Lint method, the simplest and most satisfactory is the one proposed by O'Brien⁴⁴. His description follows:

The point of the injection is just anterior to the tragus of the ear, below the posterior portion of the zygomatic process and directly over the condyloid process of the mandible. Going straight inward with a sharp needle, one strikes the bony condyloid process at a depth of about 1 cm. As soon as this bone is felt with the needle, I begin injecting 2 per cent solution of procain hydrochloride, and, gradually withdrawing, inject about 2 cc of solution. Lid paralysis begins to appear usually in from thirty to sixty seconds, and, after a very few minutes, is so marked that the patient is unable to close the lids, and the palpebral fissure is widely opened [fig 16].

⁴⁴ O'Brien C S. Local Anesthesia in Ophthalmic Surgery, Tr. Sect. Ophth., A. M. A., 1927, p. 250.

The course of the branches of the seventh nerve which supply the orbicularis muscle often varies considerably, so that paralysis is not always secured with the first injection. If, after several minutes, the action of the muscle has not been affected, another injection should be given. The point of injection should be changed slightly, the more common variations in the course of the nerve being borne in mind. The object of the injection should be accomplished before one proceeds with the operation.

Sharp pain is caused if the periosteum of the condyloid process is pricked, it should therefore be avoided. After the injection of 2 to 3 cc of the anesthetic solution, deep massage, with firm pressure over the site of the injection, will produce more rapid and complete paralysis of the orbicularis muscle.

When more prolonged paralysis of the orbicularis muscle is desired, as with patients who have a tic, with spasmodic contractions not only of the orbicularis but of other facial muscles, alcohol may be added to the solution injected.

The following solution causes little pain when injected, and the paresis lasts seven to ten days, sometimes longer: isotonic solution of sodium chloride U. S. P., 8 cc, procaine hydrochloride, 0.2 Gm., and absolute alcohol, 2 cc. Less pain will be experienced if 1.5 cc of the anesthetic solution is first injected and the syringe removed, the needle being left in place. Beginning paresis of the orbicularis muscle indicates that the needle is in the proper position. The syringe, containing the alcoholic solution, is then attached to the needle, and 1.5 cc is injected.

In selection of the method of anesthesia for any operation, the age and temperament of the patient must be considered. With the use of instillation anesthesia only, many operations on the eye may be successfully performed with no apparent discomfort in a somewhat large proportion of patients. Because of this, the surgeon often does not make use of the procedures that produce more complete anesthesia, regarding them as unnecessary and superfluous. There is, however, a small percentage of patients for whom instillation anesthesia is not sufficient or who are less stoical than others. These are the patients who so often squeeze and damage their eyes seriously or who, through inability to hold the eye quiet, make the operation more difficult. Since it is not possible before operation to select the patients who will not squeeze the eyes or who will hold well, it seems wiser for the surgeon to err on the side of caution and always obtain complete anesthesia before he begins the operation.

For all operations on the globe in which a forcible contraction of the orbicularis muscle might injure the eye this muscle should be temporarily paralyzed. Also, in operations for strabismus the procedure is made easier if the lids are relaxed. Since this can be done easily, one seems hardly justified in taking the chance of injury to the eye in this way by not obtaining paralysis of the orbicularis muscle before beginning the operation.

USE OF SEDATIVES

The careful use of sedatives before operation will assist greatly in production of a quiet, tranquil patient. The various sedatives act differently in different persons. In some they increase the excitability and may cause nausea and vomiting, so that it does not seem advisable to use any sedative, particularly in cases of operation on the globe, without one's first ascertaining the action of the drug on that particular patient. Usually the patient is admitted to the hospital at least one day before the operation. On the first night in the hospital a sedative can be given, this allows the operator not only to learn the action of the drug on that patient, but to determine whether the drug acts in the usual manner, besides, it gives the patient a quiet, restful sleep, which is excellent preliminary preparation for the operation. If there

is no undesirable reaction, it is usually safe to use the drug again before the patient goes to the operating room. Many patients, especially the older ones, are accustomed to taking a sedative, if so, it is wise to use the drug to which the patient is accustomed.

Some of the barbituric acid group, such as phenobarbital, sodium amytal and pentobarbital sodium, have a satisfactory action and rarely cause nausea or other undesirable reactions. These drugs have the effect of quieting and calming the patient, which adds greatly to the ease of the operation. Also, they have the added value of counteracting, to some extent, the toxic action of the anesthetic employed.

The dose varies somewhat for different patients. As a test dose, $1\frac{1}{2}$ grains (0.097 Gm.) of phenobarbital may be given the patient before he retires. Then, if satisfactory, a dose of from $1\frac{1}{2}$ to 3 grains (0.097 to 0.195 Gm.) may be given an hour before the operation.

APPROPRIATE METHODS OF ANESTHESIA

In the following paragraphs are listed, in alphabetical order, the different operations on the eye, with a brief indication for each operation of a method for production of complete anesthesia, previously described in detail.

Ablation of Staphyloma—Sharp pain usually accompanies the sudden decrease of intraocular tension, which often precipitates forcible contraction of the orbicularis muscle, so that complete anesthesia is desirable. An appropriate method of induction of such anesthesia consists in instillation of anesthetic (page 787), retrobulbar injection within the muscular cone (page 791), induction of akinesia (page 802) and subconjunctival injection, if the eye is inflamed (page 790).

Abcission of Prolapsed Iris—Instillation anesthesia, induction of akinesia and subconjunctival injection, since the eye is usually inflamed, are indicated. This procedure is usually sufficient, but if the eye is severely inflamed and painful and the wound is not large, injection within the muscular cone should also be made, so that when traction is exerted on the iris no pain will be experienced. The operation can then be completed leisurely and carefully, without danger to the eye.

Blepharoplasty—The method of anesthesia used will depend on the extent of the involvement and the individual features of the case. By means of infiltration anesthesia and field or nerve block, extensive plastic operations may be performed satisfactorily.

Slitting of the Canaliculus—The appropriate method consists of instillation of anesthetic (page 787) and infiltration just below the canaliculus.

Canthotomy—The appropriate method of anesthesia consists of instillation of anesthetic and infiltrations of the subcutaneous and deeper tissues between the external canthus and the orbital margin.

Canthoplasty—The same method of anesthesia as that used for canthotomy is indicated except that the lids are infiltrated as far as the operation is to extend. If the infiltration is followed by pressure and massage, there will be little distortion of the operative field. Block of the lid (page 801) may be used and thus infiltration of the operative field be avoided, but this is rarely necessary.

Capsulotomy, or Discission of the Capsule—Instillation anesthesia is usually sufficient for the discission of congenital or juvenile cataracts except with babies and young children, for whom general anesthesia is indicated. For removal of secondary or membranous cataracts, in which the capsule is thick and tough, instillation anesthesia is not sufficient. To avoid the pain caused by traction on the ciliary processes, subconjunctival injections above and below the cornea should be given. Frequently,

patients who have had a discussion with instillation anesthesia remark that they did not feel the extraction but that the needling was very painful

Extraction of Cataract—Instillation anesthesia, induction of akinesia and retrobulbar injection of the muscular cone are indicated. In cases of dislocated cataract in which the eye is inflamed and painful a subconjunctival injection should also be made to avoid production of pain when the fixation forceps is used.

Cauterization of the Cornea (ulcer, keratoconus)—Instillation anesthesia is usually sufficient except in an operation in which the cornea is to be perforated, then retrobulbar injection of the muscular cone should be made to prevent the sharp pain incident to the sudden evacuation of the anterior chamber. If the eye is inflamed, as with a corneal ulcer, a subconjunctival injection should be given to avoid production of pain when the fixation forceps is used.

Chalazion—Instillation anesthesia and injection through the conjunctiva of the cul-de-sac into the area corresponding to the chalazion (page 801) constitute the method of anesthesia.

Coloboma and Injuries of the Lids—Instillation anesthesia and block of the lid (page 801) or infiltration around the area involved are indicated.

Incision for Acute Dacryocystitis—The procedure is less painful if ethyl chloride is sprayed on a cotton applicator and applied to the site of the incision. On account of the severe induration and swelling, infiltration anesthesia or nerve block is often not advisable.

Dacryocystostomy—The method of anesthesia consists of block of the infratrochlear (page 789) and the infraorbital (page 799) nerve and use of a nasal pack.

Detachment of the Retina (microdiathermic punctures, iridopuncture)—Instillation anesthesia and injection of the muscular cone (page 791) are indicated.

Ectropion and Entropion—The method of anesthesia varies according to the operation to be performed. For cauterization, instillation and infiltration anesthesia are sufficient. For the more extensive plastic operations involving the lid, infiltration anesthesia (page 787) or block of the lid (page 801) is necessary.

Enucleation and Evisceration—Instillation anesthesia, injection of the muscular cone and subconjunctival injection, if the eye is inflamed and painful, are indicated.

Excision of the Lacrimal Gland—Instillation anesthesia and infiltration along the superior temporal margin of the orbit (page 787) are indicated.

Excision of the Lacrimal Sac—Block of the infratrochlear and the infraorbital nerve (page 798) produces complete anesthesia without any disturbance of the anatomic structures around the sac. By the infiltration method the sac can be removed without pain, but if the nasal duct is to be cuetted, pain is usually experienced. By use of pressure and massage after infiltration of the tissue over the sac, around the top of the sac and the region about the entrance of the nasolacrimal duct, the anatomic structures and landmarks are disturbed very little.

Foreign Body in the Cornea—Instillation anesthesia is indicated. One instillation is often sufficient, but the introduction of a few extra drops requires little time and adds greatly to the comfort of the patient and the ease with which the offending particle is removed, in the end it frequently saves time and epithelium.

Intraocular Foreign Body—The appropriate procedure for induction of anesthesia consists of instillation of anesthetic, induction of akinesia, injection within the muscular cone and subconjunctival injection, if the eye is red and inflamed. When a foreign body is removed through a scleral incision, a retro-

bulbar injection of the anesthetic with an added amount of epinephrine hydrochloride has the advantage of making the eye soft, so that the danger of presentation of the vitreous is lessened

Glaucoma (Cyclodialysis, Iridectomy, Iridotomy, Lagrange's Operation, Sclerotomy)—Instillation anesthesia, induction of akinesia, injection within the muscular cone and subconjunctival injection are indicated. The last injection should be made if the eye is inflamed and painful, as in cases of acute glaucoma, otherwise the use of the fixator forceps causes pain.

By the retrobulbar injection the pain incident to a sudden decrease of tension is avoided. Also, a postoperative increase in tension, due to edema of the ciliary processes, or the so-called quiet iritis, is less likely to occur. In some of the aforementioned operations production of akinesia may be superfluous, but if the patient squeezes the eye hard after the incision is made considerable damage may easily be produced, induction of akinesia does no harm and requires only a few minutes.

For the corneoscleral trephination, a 0.5 per cent solution of tetracaine hydrochloride, a 2 per cent solution of butacaine sulfate or an anesthetic that does not dilate the pupil is instilled. Epinephrine hydrochloride is not used until just before the operation is begun.

Subconjunctival injections of a 2 per cent solution of procaine hydrochloride are made at the nasal and the temporal side of the cornea and through the conjunctiva of the upper cul-de-sac deep along the superior rectus muscle.

Injection within the muscular cone gives more complete anesthesia, and if only 1 drop of epinephrine hydrochloride (1:1,000) to 10 cc of 2 per cent procaine hydrochloride is used, the tension is not lowered enough to prevent prolapse of the iris.

Induction of akinesia is advisable, as the patient's squeezing the eye after the aqueous escapes may injure the lens or cause prolapse of the ciliary processes.

Incision of Hordeolum—Although this incision is a simple procedure, it is extremely painful. A cotton applicator saturated with ethyl chloride and applied to the site of the incision renders the operation less painful. If there are not too much swelling and induration, often the lid around the hordeolum can be infiltrated so that little pain is experienced, in some cases block of the nerve or lid is most satisfactory (page 801).

Iridectomy, Iridotomy—Instillation anesthesia, induction of akinesia, injection within the muscular cone and subconjunctival injection, if the eye is inflamed and painful, are indicated. In some iridotomies in which a small incision is made in the cornea, such as that for *iris bombé*, akinesia is not necessary.

Keratoplasty—Instillation anesthesia, induction of akinesia and injection within the muscular cone are indicated. As cocaine somewhat devitalizes the cornea, its use may account for some of the grafts' becoming cloudy. For this operation use of other anesthetic agents for instillation, such as tetracaine, seems advisable.

Kronlein Operation—While this operation is usually performed with the patient under general anesthesia, it may also be done with local anesthesia, just as are many intracranial operations.

The type of anesthesia to be used depends to a great extent on the orbital involvement. With large orbital tumors, particularly vascular growths, an orbital block is not advisable. With small tumors, or when the operation is done to relieve exophthalmos, the procedure may be accomplished with a field block surrounding

the area of operation After the bone flap has been raised, intraorbital injections can be used as necessary, the indication depending on the amount of orbital interference

Operations on Muscles (Advancement, "Cinching" or Tucking Operations, Recession, Resection)—Instillation of anesthetic and injection within the muscular cone constitute the method used The paresis of the muscles caused by the retrobulbar injection is an objection but is not so serious as with general anesthesia However, before the operation the surgeon has usually estimated the amount of correction necessary and has decided on just how much advancement, resection or recession of the muscle he will produce, so that the paresis is not a serious handicap A deep injection may be made along the muscle, but it does not prevent the pain caused by traction on other muscles, and frequently the injected solution balloons the surrounding tissues, so that the operation is made more difficult Also, an injection within the cone is as easy and safe as a deep injection along the muscle

Tenotomy of the rectus muscles can be performed satisfactorily with instillation anesthesia, but usually it causes some pain, which can be avoided by either injection within the muscular cone or injection in the vicinity of the muscle to be tenotomized, if massage with pressure is employed, the anatomic relations are not disturbed enough to interfere with a satisfactory tenotomy

Tenotomy of the Inferior Oblique Muscle—1 A wheal is raised in the vicinity of the inferior nasal margin of the orbit (page 789) 2 Tissues beneath the skin and the deeper tissues along the orbital margin in the vicinity of the attachment of the inferior oblique muscle are infiltrated (page 787) If the tenotomy is to be done through the conjunctiva, instillation anesthesia should be used, and the injection along the orbital margin may be made through the conjunctiva of the lower cul-de-sac

Opticociliary Neurotomy—The method employed is instillation of anesthetic, injection within the cone and subconjunctival injection, since the eye is usually inflamed and painful

Paracentesis of the Cornea and Sclera—The eye is usually inflamed, and the operation, although simple, is generally extremely painful unless complete anesthesia is obtained The method consists in instillation of anesthetic, injection within the muscular cone, subconjunctival injection, if the eye is inflamed (otherwise the use of fixation forceps is painful), and, in some cases, induction of akinesia

Plastic Operations—Since plastic operations vary to such a degree with each patient, it is not practical to attempt to outline a definite procedure for induction of anesthesia While some extensive plastic operations require general anesthesia, many can be performed with local anesthesia by means of infiltration, nerve block and field block (page 789) Scar tissue cannot be satisfactorily infiltrated, but unless it is extensive, the area can usually be rendered anesthetic by the use of field or nerve block

Probing of the Lacrimal Duct—Instillation anesthesia and the injection of several drops of the anesthetic solution into the lacrimal sac somewhat relieve the pain but block of the infratrochlear and the anterior superior alveolar nerve (page 796) renders the procedure practically painless For passage of small probes, in which little pressure is exerted, instillation into the conjunctival and lacrimal sacs is usually sufficient, but insertion of a large probe, if anesthesia is not adequate, is usually very painful

Pterygium—Instillation anesthesia and subconjunctival injection under the pterygium, and below the cornea if transplantation is to be made below, are indicated

Ptosis—The operations for ptosis are numerous, but the majority can be performed with the aid of local anesthesia, particularly if the patient is not too young.

Here, again, the procedure for induction of anesthesia depends on the operation to be performed. For operations that involve the superior rectus muscle, such as the Mott's operation, the following procedure is adequate: instillation of anesthetic, injection within the muscular cone, subconjunctival injection into the upper cul-de-sac and infiltration under the skin of the lid, where the sutures pass through the skin.

Saemisch's Keratotomy—Instillation anesthesia, injection within the cone and subconjunctival injection, to avoid pain on use of the fixation forceps, are adequate.

Tattooing—Instillation anesthesia is adequate.

Trachoma—Expression. Instillation anesthesia and subconjunctival injection into the cul-de-sac of a large amount of anesthetic solution are indicated. In young children and in some adults general anesthesia is usually necessary, as the operation is extremely painful.

Combined Excision of Fornix and Tarsus. Instillation anesthesia and subconjunctival injection of a large amount of anesthetic solution into the cul-de-sac are adequate.

CONCLUSION

Practically all ophthalmic operations may be painlessly and safely performed with use of local anesthesia provided the anesthetic is carefully and properly administered.

Correspondence

EMMETROPIA

To the Editor —The concept of emmetropia, though it is fundamental in the ophthalmologist's work, is hardly as simple and fixed as textbook definitions seem to imply. As evidence of this one may refer to an article by Dr Edwin S. Munson (Emmetropia, *ARCH OPTH* 29: 109 [Jan] 1943). Several points relative to emmetropia not touched on in that article are, I believe, of sufficient interest to be mentioned.

The aberrations of the eye play an important role not only in determination of visual acuity but in the very definition of emmetropia. Gullstrand, for example, made his emmetropic eye 1.00 D hyperopic for paraxial rays. To understand fully the implication of this, one must visualize how the light from an object point is acted on by the eye as the light passes through the different mediums. In essence, every pencil of light from an object which passes through the pupil reaches the vitreous as a more or less irregular, cone-shaped bundle of rays—call it conoid for short—the impact of which on the retina produces a diffusion spot. The rays which compose the outer layers of the conoid form innumerable and variously placed focal points with one another before and after they strike the axis. The aggregate of these multiple and scattered focal points form the so-called caustic. In the usual positive spherical aberration, the rays immediately around the axis, the so-called paraxial rays, focus farther back on the axis than the marginal rays, those passing through the edge of the pupil.

The cross section of the conoid where it strikes the retina forms a diffusion spot, in which the concentration of light will never be uniform throughout. The spot differs in size, shape and brightness distribution according to the section of the conoid intercepted by the retina. Somewhere between the axial focus of the marginal rays and the axial focus of the paraxial rays is the "circle of least confusion." This forms the narrowest part, or the "waist," of the conoid. If the retina intercepts the conoid at or near the marginal focus (therefore in front of the circle of least confusion), the diffusion patch on the retina will show the greatest concentration of light near the periphery of the patch. If the retina intercepts the conoid at or near the paraxial focus, the diffusion patch on the retina will show the greatest concentration of light near the center of the patch. If the retina intercepts the conoid at the circle of least confusion, the difference between the light and the dark areas in the patch is generally least and the patch is more nearly uniformly bright.

It seems that the cross section of the conoid which gives best vision, and to which the eye tends to adapt itself, varies not only in different persons but in the same person, the section depending on the nature of the object viewed. Gullstrand stated that the eye adapts itself to a section of the conoid about 1 D in front of the paraxial focus. Therefore his "emmetropic" eye, emmetropic in the sense that it is best adapted for clear distant vision on the usual charts, has 1 D of hyperopia for paraxial rays.

On the other hand, examination by the ophthalmoeikonometer shows that an eye which has been made emmetropic in the sense that it is best adapted for distant vision on the Snellen chart is about 0.50 D myopic for a target consisting of a minute point of light. This can be explained on the supposition that when made "emmetropic" for the Snellen chart the eye chooses a section of the conoid at or near the paraxial focus, where the greatest concentration of light is near the center, but when focusing on a bright point of light it chooses a section of the conoid corresponding to the "waist," or circle of least confusion. This point is about 0.50 D in front of the paraxial focus. Luckiesh and Moss, in making tests with an instru-

ment of their own invention, the sensitometer, stated "In the typical emmetropic subject, during a state of complete rest, the eyes are about 0.75 D myopic." This bears out the findings of the Dartmouth school. This discrepancy they explained on the basis of negative relative accommodation, more likely it is due to the eye's choosing a different section of the conoid for best vision of different targets.

Thus the concept of emmetropia based on what actually takes place in the act of seeing involves consideration of the methods of testing, the size of the pupil ("An eye that was emmetropic with a pupil of medium size would have to show hypermetropia amounting to 1 diopter with an infinitely small pupil" [Gullstrand]), the nature of the test object, the relative illumination of the test object and the background and possibly other factors. One of the best articles on the effect of the retinal diffusion patches on vision and visual acuity is a paper by Dr. Walter B. Lancaster (Stigmatoscopy, *Tr Am Ophth Soc* 32: 130, 1934). The discussion and illustrations, presented in Dr. Lancaster's lucid, inimitable way, will be an eye opener to persons whose concept of emmetropia is based on the old, familiar diagram of parallel rays meeting at the retina.

JOSEPH I. PASCAL, M.D., New York

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CONVERSION FORMULA FOR SNELLEN SYMBOLS

To the Editor—Dr. Gabriel's equations, which appeared in the July issue (*ARCH OPHTH* 30: 138, 1943) are simple and correct for conversion from the Snellen to the Navy terminology. Why not make the method still simpler?

$$\begin{aligned} 6/7.5 &= 20/25 = 4/5 = 7/20 = 16/20 \\ 20/30 &= 2/3 = 7/20 = 13/20 \end{aligned}$$

This soon forms a picture in the examiner's brain, and the process becomes semiautomatic.

D. G. ALLEN, M.D., Cleveland

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News and Notes

GENERAL NEWS

American Board of Ophthalmology—An examination will be held in New York on June 3 and 4, 1944 and in Chicago on Oct. 5, 6 and 7, 1944.

Further information with respect to examinations may be obtained from the secretary-treasurer, Dr. S. Judd Beach, P. O. Box 1940, Portland 2, Maine.

The other officers for 1944 are: chairman, John Green, M.D., St. Louis; vice chairman, Frederick C. Cordes, M.D., San Francisco; and assistant secretary, Theodore L. Terry, M.D., Boston.

Ophthalmic Gold Medal—The Ophthalmological Society of Egypt offers a yearly prize, consisting of a gold medal of the value of £20 (English), for the most valuable contribution presented before the annual congress of the society. This competition is open to members of the society, and the manuscript is to be sent in by December.

SPECIAL NEWS

Course for Orthoptic Technicians—The Rochester (N. Y.) Orthoptic Center (approved by the Monroe County Medical Society) offers a course for orthoptic technicians. Young women desirous of making orthoptics a career and of preparing for the examinations of the American Orthoptic Council may get full particulars from Mrs. Margaret Lundean, orthoptic technician, 31 North Goodman Street, Rochester, N. Y.

Abstracts from Current Literature

EDITED BY DR WILLIAM ZENTMAYER

Anatomy and Embryology

- A QUANTITATIVE STUDY OF THE CELLS AND FIBERS IN THE NUCLEUS NERVE COMPLEXES OF THE FOURTH AND SIXTH CRANIAL NERVES R D HARLEY, *Am J Ophth* 25:1029 (Sept) 1942

Harley collected specimens of the nerves and nuclei from 32 normal human brains. From a study of these specimens, he concludes

"Since there are clearly more cells in the so-called nuclei than motor fibers in the peripheral nerves, it is logical to assume that the motor nuclei of the fourth and sixth cranial nerves send fibers not only peripherally into these nerves, but centrally to other regions, such as to other cranial nuclei, probably via the median longitudinal fasciculus. Some of the association mechanism (association centers) may thus be within the confines of the so-called nuclei of the ocular nerves."

W S REESE

- THE AQUEOUS VEINS K W ASCHER, *Am J Ophth* 25:1174 (Oct) 1942

In his summary, Ascher states that aqueous veins are biomicroscopically visible pathways with appearance of blood vessels, containing a clear, colorless fluid or diluted blood and intercalated, probably via Schlemm's canal, between intraocular fluid, on the one side, and conjunctival and subconjunctival veins, on the other. Anatomically they are connected with, or are a part of, the intrascleral network. He describes tests that prove this and expresses the opinion that these aqueous veins confirm Leber's theory of a continuous elimination of fluid from the intact human eye.

W S REESE

Aqueous Humor

- THE INTRASCLERAL VASCULAR PLEXUS AND ITS RELATIONS TO THE AQUEOUS OUTFLOW M U TRONCOSO, *Am J Ophth* 25:1153 (Oct) 1942

Troncoso compares the anatomy of the anterior chamber of different species of animals. He concludes that in primates there is not a blood-aqueous barrier and that aqueous passes directly through the collectors into the blood stream.

W S REESE

- SULFONAMIDE CONTENT OF AQUEOUS HUMOR FOLLOWING CONJUNCTIVAL APPLICATION OF DRUG POWDERS E GALLARDO and R THOMPSON, *Am J Ophth* 25:1210 (Oct) 1942

Gallardo and Thompson give the following summary

"Acute inflammation produced by mustard oil [allyl isothiocyanate] in the conjunctiva or by streptococcal infection of the anterior chamber increased the passage of sulfanilamide into the aqueous fluid. The increase may have been due entirely to injury of the corneal epithelium, since intraocular inflammation by the intravenous injection of killed typhoid bacilli definitely diminished passage of the drug. Even with this inflammation, however, effective aqueous fluid concentrations could often be demonstrated.

"Of the drugs tested by local application, the higher levels in the aqueous humor were obtained with sulfanilamide."

W S REESE

Conjunctiva

ACUTE FOLLICULAR CONJUNCTIVITIS RESEMBLING BEAL'S TYPE M P KOKE,
Am J Ophth 25: 1100 (Sept) 1942

Koke describes an epidemic of acute follicular conjunctivitis among 66 aircraft workers. The cardinal characteristics of the disease were (1) acute or subacute unilateral onset with profuse lachrymation, (2) absence of exudate, (3) severe hyperemia of the conjunctiva, (4) folliculosis, which was most marked in the conjunctiva of the inferior fornix, (5) slightly tender preauricular adenitis, (6) swelling of the lids, (7) complete resolution in seven to twenty-one days, (8) absence of inclusion bodies or pathogenic bacteria in scrapings from the conjunctiva, and (9) abundance of lymphocytes in the conjunctival scrapings. Seven patients showed superficial keratitis. Koke suggests that this condition is due to a virus.

W S REESE

Congenital Anomalies

A RARE CONGENITAL OCULAR ABNORMALITY G S PENDSE, Indian J Ophth
4: 1 (Jan) 1943

A girl, born at full term, would not open her eyes at birth, and examination revealed absence of the eyeballs though a bluish swelling within the right orbit showed that the condition was not anophthalmos. Examination a few weeks later showed that the swelling was increasing under the skin, which was bluish, and revealed another swelling in the left lower lid. Transillumination revealed that both were transparent. There were no other ocular or extraocular abnormalities. The diagnosis of bilateral microphthalmos with cysts, though the most probable one, cannot be verified without pathologic examination of the cysts. The article is illustrated.

W ZENTMAYER

Cornea and Sclera

CORNEAL PERMEABILITY K C SWAN and N G WHITE, Am J Ophth 25:
1043 (Sept) 1942

Swan and White describe their experiments on corneal permeability and state that permeability is not a simple matter of diffusion but a complex process affected by multiple interrelated factors and that the concept that the epithelium acts as a barrier limiting the penetration of all substances into the cornea is erroneous. They conclude:

"In evaluation of the ocular effects of drugs administered by instillation, penetration rate under varying conditions as well as pharmacologic potency must be considered. The difference in effectiveness of topical anesthetics may be due principally to differences in penetration rate into the cornea."

W S REESE

EPIDEMIC KERATOCONJUNCTIVITIS M J HOGAN and J W CRAWFORD, Am J
Ophth 25: 1059 (Sept) 1942

Hogan and Crawford give the following summary and conclusions:

"This paper reports the occurrence of a severe epidemic of keratoconjunctivitis occurring in, but not limited to, shipyard workers. In all 125 cases are reported.

"The disease we have described is a superficial keratoconjunctivitis which, because of its epidemic form, should be called epidemic keratoconjunctivitis. This disease has been described under various names such as keratitis nummularis (Dimmer) and some forms of keratitis disciformis associated with superficial macular lesions. From its appearance and history the disease suggests a relationship to Béal's form of conjunctivitis. Superficial epithelial erosions should not be classed with the disease under discussion.

There is great variation in the clinical picture, even during epidemics. Seventy-five per cent of the conjunctival infections are unilateral. Diagnostic in the early states are the glassy edema of the conjunctiva, involvement of the regional lymph apparatus, the lymphocytic type of conjunctival exudate, tiny petechial hemorrhages, pseudomembrane formation, and the lack of discharge. The severe conjunctivitis may or may not be followed by keratitis. Keratitis occurs in about 75 per cent of the cases, though this figure varies in different epidemics. At times keratitis occurs without a history of preceding conjunctivitis.

"The disease is most likely caused by a virus, the nature of which is unknown but which may be related to the herpes-facialis group. The disease is not highly infectious. It is transmitted by direct contact to susceptible persons, and individual susceptibility varies.

"Therapy is of little avail except possibly in the early stages and in milder cases. The disease is self-limited.

"The ultimate prognosis is good as regards vision."

W S REESE

Experimental Pathology

LYMPHOGRANULOMA-VENEREUM LESIONS OF THE EYES. C ESPÍLDORA and W E COUTTS, *Am J Ophth* 25:916 (Aug) 1942

The authors review the literature concerned with experimental lesions in animals and lesions in man and make the following conclusions:

"(1) The eye may be the site of lymphogranuloma-venereum lesions during any one of the periods of this disease.

"(2) Any structure of the eye may be involved by the process.

"(3) All structures in direct contact with the exterior may serve as the site of inoculation for the virus of lymphogranuloma venereum."

W S REESE

General Diseases

THE RELATION OF RIBOFLAVIN TO THE EYE. A PIRIE, *Brit J Ophth* 27:291 (July) 1943

The subject is reviewed under the following heads: properties of riboflavin, occurrence of riboflavin in the body, flavoprotein enzymes, and relation of riboflavin to the eye, general effects of riboflavin deficiency in animals, and effects of deprivation of riboflavin on the eyes of experimental animals.

Pirie considers it extremely interesting that the ocular signs of riboflavin deficiency are among the earliest to develop and may be used in conjunction with changes in the skin and tongue in making an early diagnosis of the deficiency.

W ZENTMAYER

Glaucoma

ROENTGEN THERAPY OF GLAUCOMA. M F TERRIZZANO and A M J TERRIZZANO, *Semana méd* 49:1354 (Dec 3) 1942

The Terrizzanos employed roentgen irradiation in 10 cases of glaucoma. In 1 case the disease was of traumatic origin, in 6 it was painful and chronic, in 2 hemorrhages occurred, and in 1 the glaucoma was accompanied by hypertensive iritis. Improvement resulted in all cases. Pain and lacrimation either disappeared or improved. Keratoconjunctival inflammation disappeared rapidly, and no disagreeable reaction was observed. In only 1 of the 10 cases did a relapse occur, after seven months, and two new irradiations were effective in counteracting the condition. The authors suggest that the effect of roentgen therapy is due to complex action on intraocular osmotic phenomena, modifications in the capillary circulation, tissue ionization, variations in the acid-base and colloid equilibrium.

and direct action on the neural terminations Irradiation using a tension of 140 kilovolts, with 10 milliamperes, at a distance of 50 cm and filtration through 0.25 mm of copper and 1 mm of aluminum gives the best results

J A M A (W ZENTMAYER)

Injuries

TETANUS FOLLOWING EYE INJURY J O WETZEL, *Am J Ophth* 25 933 (Aug) 1942

Wetzel reports the case of a farmer who sustained a perforating laceration of the eyeball, with prolapsed iris, as a result of an injury from a nail while he was working in his barn Tetanus developed, but he recovered, the eye having been enucleated Wetzel reviews 30 case reports in the literature and urges the routine use of tetanus antitoxin because of the high mortality

W S REESE

PIECE OF GLASS MOVABLE IN THE EYEBALL FOR TWENTY-THREE YEARS REPORT OF A CASE R CAUER, *Klin Monatsbl f Augenh* 106:91 (Jan) 1941

The rimless nose-glass of a youth aged 15 was struck by a toy arrow and a splinter entered his eye A penetrating wound was observed in the sclera 9 mm nasal to the limbus Apparently complete recovery with perfect vision was obtained two months later No trace of the splinter could be observed after the vitreous had cleared The patient returned after twenty-two years, during which period his eye had been free from any disturbance Vision in that eye had become blurred, and congestion was noted on the morning of his visit A few days later the splinter, 4 mm long, presented at the floor of the anterior chamber It had slowly traveled a distance of 9 mm The eye recovered promptly after extraction of the splinter

K L STOLL

LOCALIZATION OF FOREIGN BODIES IN POSTERIOR WALL OF THE EYEBALL, AND THEIR OPERATIVE REMOVAL BY USE OF THE SCLERAL LAMP REPORT OF A CASE H COLDITZ, *Klin Monatsbl f Augenh* 106:94 (Jan) 1941

The increasing frequency of nonmagnetic foreign bodies in the eye requires new methods for their removal A number of these technics are discussed and evaluated Colditz describes his own method, by means of which he extracted a piece of copper, a portion of the cartridge, from the eye of a patient It had been in the eye about five weeks and had produced exudation in the periphery of the fundus, decrease of vision and contraction of the field of vision The new method, consisting of inflation of air into Tenon's capsule and simultaneous use of Comberg's prothesis, allows exact intrabulbar and extrabulbar localization of splinters Diascleral illumination proved of great value The splinter was removed, as described in detail, and perfect recovery was obtained, with four-fifths normal vision and a normal field of vision

K L STOLL

Lens

NOTE ON INTRACAPSULAR EXTRACTIONS OF CATARACT BY WEBER'S LOOP AS A ROUTINE METHOD D D SATHAYE, *Indian J Ophth* 4:9 (Jan) 1943

The usual corneal incision is made with a long, narrow conjunctival bridge above, and iridectomy is performed A Weber loop is introduced and directed obliquely backward through the incision until it reaches a point in the middle of the vitreous and about opposite the posterior pole of the lens By depression of its handle, it is then carried forward, so that the lens is pressed against the posterior surface of the cornea, between the cornea and the loop In other words, the

lens is lifted out of the eye by the loop. This method has been used in a series of 38 consecutive cases, with good results. In 1 case there was an excessive escape of vitreous, and in another case the capsule of the lens was ruptured.

The article is well illustrated.

W ZENTMAYER

Ocular Muscles

RECESSION OF THE TROCHLEA IN OVERACTION OF THE SUPERIOR OBLIQUE W L HUGHES and D W BOGART, *Am J Ophth* 25:911 (Aug) 1942

Hughes and Bogart briefly discuss overaction of the superior oblique muscle and suggest a simple effective operation of recession of the trochlear as a remedy. Two cases are reported.

W S REESE

EXPERIMENTAL TRANSPOSITION OF EXTRAOCULAR MUSCLES IN MONKEYS P J LEINFELDER and N M BLACK JR, *Am J Ophth* 25:974 (Aug) 1942

This is the authors' second article on this subject, and they conclude that the superior oblique muscle alone does not appear to have any special coordinating function that cannot be ascribed to any other muscle. They suggest there may be a relation between the amount of involvement of Tenon's capsule in surgical intervention and recovery of coordination.

W S REESE

Orbit, Eyeball and Accessory Sinuses

THROMBOPHLEBITIS OF THE CAVERNOUS SINUS RECOVERY A R C DOORLY, *Brit M J* 1:42 (Jan 9) 1943

A healthy married woman aged 56 had a nasal furuncle inside the left nostril. There was the usual edematous swelling of the adjacent cheek, with intense pain and slight fever. She was treated with sulfathiazole, one tablet (0.5 Gm) every four hours, and glycerin packs were advised for the interior of the nose. On the following day there was more swelling, the temperature was 101 F and pus was being discharged from the furuncle. Two days later the left eye was proptosed, both lids were greatly swollen and the right eye was commencing to be involved. The patient complained of seeing double on looking to the left. There was some rigidity of the neck muscles, and the temperature rose to 103 F. A blood culture showed *Staphylococcus aureus* of the same type as that found in the nasal lesion. She was treated with transfusion of 400 cc of whole blood and intramuscular injection of sulfathiazole (2-[paraaminobenzenesulfonamido]-thiazole) alternating with oral administration of the drug, 4 Gm being given by each route within the first twenty-four hours. After two days the temperature began to fall and the general condition improved. The chemotherapy was continued, though after three days the dose was reduced. The next day there was a sharp rise of temperature, and a second transfusion of blood was given. This was followed by improvement, but there was a third relapse. Another blood transfusion was given and the sulfathiazole treatment continued. During the next four days the patient remained very ill with an extensive rash and severe headache, but the local condition of the eyes showed improvement. As the rash was so distressing and the patient by then had taken 95 Gm of sulfathiazole, the chemotherapy was discontinued. After this the temperature gradually came down, the rash faded and the swelling left the lids. Headache gradually ceased, and convalescence began.

It has been generally recognized that free incision is dangerous and apt to lead to rapid dissemination of the infection. Hence the method of treatment reported, offering a good chance of recovery, is extremely gratifying. It is difficult to say whether the blood transfusions or the sulfathiazole played a greater part in the cure of the condition but the author thinks the combination important. The case proved conclusively the great value of sulfathiazole in the treatment of

serious staphylococcic infections and showed that the toxicity of this drug is only half that of sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine)

ARNOLD KNAPP

Tumors

FIVE HUNDRED MELANOMAS OF THE CHOROID AND CILIARY BODY FOLLOWED FIVE YEARS OR LONGER G R CALLENDER, H C WILDER and J E ASH, *Am J Ophth* 25 962 (Aug) 1942

The authors give the following summary of their article

"There are 1,600 cases of malignant intraocular melanoma on record in the American Registry of Ophthalmic Pathology Only eight of these are in Negroes There is a slight preponderance of males over females The tumor is one peculiar to adult life and appears but rarely in the earlier decades Five hundred patients suffering from melanoma of the choroid and ciliary body have been followed five years or longer, or have died as a result of metastases before the expiration of that time The tumors in this group have been classified by cell type and fiber content, and the following corollaries have been drawn The pure spindle-cell types, particularly subtype A, are of a relatively low degree of malignancy, and an increased degree of malignancy is associated with the presence of epithelioid cells, a low degree of malignancy is usually associated with a heavy fiber content

"Although there appears to be an increased lethality with increased pigment content, it is felt that there is not enough variation in death percentages to justify conclusions until a larger number of followed cases has been accumulated The total number of metastatic deaths is 239 among the cases followed five years or longer, or 48 per cent This percentage increased to 66 in 200 of these cases followed 10 years or longer "

W S REESE

Vision

COMPARISON OF CASES OF ATYPICAL AND TYPICAL ACHROMATOPSIA L L SLOAN and S M NEWHALL, *Am J Ophth* 25.945 (Aug) 1942

Sloan and Newhall report their studies on 3 cases of achromatopsia They discuss the different varieties of this condition and comment on the possible causes and the theories which have been advanced to explain them

W S REESE

MEASURE OF NIGHT VISION N B HARMAN, *Brit M J* 1:43 (Jan 9) 1943

There are several tests for night vision Some are distinctly ingenious, but with some there is no definite measure of the minimum light necessary for vision in the particular subject tested, which the author regards as the most important point This measure should be given by a direct reference to the scientific standard of candle power, and it should be ascertained and recorded in terms which can be used by any ophthalmic surgeon who repeats the process

The earliest tests of night vision measured the time required by the subject to become adapted to the dark, but adaptation tests do not give a definite measure of the minimum light required to see an object or objects The objection to Dr W D Wright's and Major Rycroft's tests is that they do not give a definite measure of the lighting, so that the results are not exactly comparable

The disk-spotting test (Harman, N B Testing Night Vision, *Brit M J* 2:347 [Sept 6] 1941) is planned on a direct measurement of light The light is reflected from illuminated disks on a black velvet background, and the measure is gained by finding the distance at which the disks can be counted This distance is designated in fractions of 5, and the fractional figure indicates the condition of the patient's night vision, which is fully explained in this article The illumination is from the standard candle, so that there is exactness of the light used and of its measurement and the returns of the examination are definite

ARNOLD KNAPP

Book Reviews

A Hundred Years of Medicine By C D Haagensen and Wyndham E B Lloyd Price, \$3.75 Pp 444, with 42 illustrations New York Sheidan House, Inc , 1943

This book was first published in an English edition by Dr Wyndham E B Lloyd, a specialist in public health in England, and now appears in an American edition. The important medical advances are traced through the years, and to simplify the presentation the authors consider each contribution to medicine separately. The American edition differs much from the preceding one, while part I, which deals with the historical background, and chapters 10 to 19 of part II, on infectious diseases, by Dr Lloyd, are unchanged except for some additions, the rest of this new edition has been rewritten by the American editor, Dr C D Haagensen, surgeon and pathologist to Columbia University College of Physicians and Surgeons.

"A Hundred Years of Medicine" is written especially for the layman and the beginner in medicine. The authors have admirably succeeded in presenting a book "on the face of diseases," relieved of the dry facts of anatomy, physiology and pathology, which should appeal to the beginner and can be read with interest by the practicing physician, especially by one, like the specialist, whose work has become confined to narrower lines. The book is divided as follows: part I, medicine up to a hundred years ago, part II, medical science during the last hundred years, part III, surgery during the last hundred years, and part IV, the new social aspect of medicine, with a bibliography and an index in conclusion.

It is difficult to pick out outstanding chapters, as all are excellent. The facts are presented in an unusually interesting manner so that the reading becomes fascinating and absorbing. The subjects are completely and successfully presented and the personalities who took an active part in the remarkable development of medicine are admirably described. The book ends with a view to the future, and the difficulties and advantages of group practice are discussed. This book is a fascinating contribution to medical history and can be highly recommended.

ARNOLD KNAPP

CORRECTION

In the article by Dr Otto Lowenstein and Dr Isadore Givner entitled "Pupillary Reflex to Darkness," in the November issue (*ARCH OPHTH* 30: 603, 1943), the term "rotary nystagmus" in line 20 on page 608 should read "retraction nystagmus."

Directory of Ophthalmologic Societies *

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Place Peiping Union Medical College, Peiping Time Last Friday of each month

GERMAN OPHTHALMOLOGICAL SOCIETY

President Prof W Lohlein, Berlin

Secretary Prof E Engelking, Heidelberg

HUNGARIAN OPHTHALMOLOGICAL SOCIETY

President Prof I Iwre, Budapest

Assistant Secretary Dr Stephen de Grosz, University Eye Hospital, Mariautca 39, Budapest

All correspondence should be addressed to the Assistant Secretary

MIDLAND OPHTHALMOLOGICAL SOCIETY

President Dr W Niccol, 4 College Green, Gloucester, England

Secretary Mr T Harrison Butler, 61 Newhall St, Birmingham 3, England

Place Birmingham and Midland Eye Hospital

*Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date

NORTH OF ENGLAND OPHTHALMOLOGICAL SOCIETY

President Dr A MacRae, 6 Jesmond Rd, Newcastle-upon-Tyne, England
 Secretary Dr Percival J Hay, 350 Glossop Rd, Sheffield 10, England
 Place Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation
 Time October to April

OPHTHALMOLOGICAL SOCIETY OF AUSTRALIA

President Dr A James Flynn, 135 Macquarie St, Sydney
 Secretary Dr D Williams, 193 Macquarie St, Sydney

OPHTHALMOLOGICAL SOCIETY OF EGYPT

President Prof Dr Mohammed Mahfouz Bey, Government Hospital, Alexandria
 Secretary Dr Mohammed Khalil, 4 Baehler St, Cairo
 All correspondence should be addressed to the secretary, Dr Mohammed Khalil

OPHTHALMOLOGICAL SOCIETY OF THE UNITED KINGDOM

President Mr T Harrison Butler, 61 Newhall St, Birmingham 3, England
 Secretary Mr L H Savin, 7 Queen St, London, W 1, England

OPHTHALMOLOGY SOCIETY OF BOMBAY

President Dr D D Sathaye, 127 Girgaum Rd, Bombay 4, India
 Secretary Dr H D Dastur, Dadar, Bombay 14, India
 Place H B A Free Ophthalmic Hospital, Parel, Bombay 12 Time First Friday of every month

OXFORD OPHTHALMOLOGICAL CONGRESS

Master Mr P G Doyne, 60 Queen Anne St, London, W 1, England
 Secretary-Treasurer Dr F A Anderson, 12 St John's Hill, Shrewsbury, England
 Place Oxford, England Time July 8-9, 1943

PALESTINE OPHTHALMOLOGICAL SOCIETY

President Dr Arich Feigenbaum, Abyssinian St 15, Jerusalem
 Secretary Dr E Sinai, Tel Aviv

POLISH OPHTHALMOLOGICAL SOCIETY

President Dr W. Kapuściński, 2 Waly Batorego, Poznań
 Secretary Dr J Sobański, Lindley'a 4, Warsaw
 Place Lindley'a 4, Warsaw

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President Col F A Juler, 96 Harley St, London, W 1, England
 Secretary Dr Harold Ridley, 60 Queen Anne St, London, W 1, England

SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President Dr W Belfort Mattos, Caixa Postal, 4086, São Paulo, Brazil
 Secretary Dr Silvio de Almeida Toledo, Enfermaria Santa Luzia, Santa Casa de Misericórdia, Cesario Motta, St 112, São Paulo, Brazil

SOCIEDAD ARGENTINA DE OFTALMOLOGIA

Chairman Dr Jorge Malbrán, Buenos Aires
 Secretary Dr Benito Just Tiscornia, Santa Fe 1171, Buenos Aires

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President Prof Dr Carlos Weskamp, Laprida 1159, Rosario
 Secretary Dr Juan M Vila Ortiz, Cordoba 1433, Rosario
 Place Rosario Time Last Saturday of every month, April to November, inclusive
 All correspondence should be addressed to the President

SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President Dr Theonilo Amorim, Barra Avenida, Bahia, Brazil
 Secretary Dr Adroaldo de Alencar, Brazil
 All correspondence should be addressed to the President

SOCIETÀ OTTALMOLOGICA ITALIANA

President Prof Dott Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome
 Secretary Prof Dott Epimaco Leonardi, Via del Gianicolo, 1, Rome

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary Dr René Onfray, 6 Avenue de la Motte Picquet, Paris, 7^e

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President Prof K G Ploman, Stockholm
 Secretary Dr K O Granstrom, Sodermalmstorg 4 Ill tr, Stockholm, So

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President Dr D Arieh-Friedman, 96 Allenby St, Tel Aviv, Palestine
 Secretary Dr Sadger Max, 9 Bialik St, Tel Aviv, Palestine

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY,
SECTION ON OPHTHALMOLOGY

Chairman Dr Conrad Berens, 35 E 70th St, New York City
 Secretary Dr R J Masters, 23 E Ohio St, Indianapolis
 Place Chicago Time June 12-16, 1944

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY,
SECTION ON OPHTHALMOLOGY

President Dr James A Babbitt, 1912 Spruce St, Philadelphia
 President-Elect Dr Lawrence T Post, Metropolitan Bldg, St Louis
 Executive Secretary-Treasurer Dr William L Benedict, 101-1st Ave. Bldg, Rochester, Minn

AMERICAN OPHTHALMOLOGICAL SOCIETY

President Dr John Green, 3720 Washington Ave, St Louis
 Secretary-Treasurer Dr Walter S Atkinson, 129 Clinton St, Watertown, N Y
 Place Hot Springs, Va Time May 29-31, 1944

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC

Chairman Dr Frederick C Cordes, 384 Post St, San Francisco
 Secretary-Treasurer Dr Brittain F Payne, School of Aviation Medicine, Randolph Field,
 Texas

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President Dr Alexander E MacDonald, 170 St George St, Toronto
 Secretary-Treasurer Dr L J Sebert, 170 St George St, Toronto

CANADIAN OPHTHALMOLOGICAL SOCIETY

President Dr Colin A Campbell, 170 St George St, Toronto
 Secretary-Treasurer Dr Kenneth B Johnston, Suite 1, 1509 Sherbrooke St W, Montreal

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President Mr Mason H Bigelow, 1790 Broadway, New York
 Secretary Miss Regina E Schneider, 1790 Broadway, New York
 Executive Director Mrs Eleanor Brown Merrill, 1790 Broadway, New York

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON
EYE, EAR, NOSE AND THROAT

President Dr N Zwaifler, 46 Wilbur Ave, Newark
 Secretary Dr William F Keim Jr, 25 Roseville Ave, Newark
 Place 91 Lincoln Park South, Newark Time 8 45 p m, second Monday of each month,
 October to May.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr L J Friend, 425 E Grand Ave, Beloit, Wis
Secretary Dr G L McCormick, 626 S Central Ave, Marshfield

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President Dr Paul A Chandler, 5 Bay State Rd, Boston
Secretary-Treasurer Dr Merrill J King, 264 Beacon St, Boston
Place Massachusetts Eye and Ear Infirmary, 243 Charles St Boston Time 8 p m, third
Tuesday of each month from November to April, inclusive

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President Dr D H O'Rourke, 1612 Tremont Pl, Denver
Secretary-Treasurer Dr C Allen Dickey, 450 Sutter St, San Francisco

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr L L McCoy, 1317 Marion St, Seattle, Wash
Secretary-Treasurer Dr Barton E Peden, 301 Stimson Bldg, Seattle
Place Seattle or Tacoma, Wash Time Third Tuesday of each month except June July and
August

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President Dr J Sheldon Clark, 27 E Stephenson St, Freeport, Ill
Secretary-Treasurer Dr Harry R Warner, 321 W State St, Rockford, Ill
Place Rockford, Ill, or Janesville or Beloit, Wis Time Third Tuesday of each month from
October to April, inclusive

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr M H Pike, Midland, Mich
Secretary-Treasurer Dr R H Criswell, 407 Phoenix Bldg, Bay City, Mich
Place Saginaw or Bay City, Mich Time Second Tuesday of each month, except July and
August

SIoux VALLEY EYE AND EAR ACADEMY

President Dr J C Decker, 515 Francis Bldg, Sioux City, Iowa
Secretary-Treasurer Dr J E Dvorak, 408 Davidson Bldg, Sioux City, Iowa

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman Dr John H Burleson, 414 Navarro St, San Antonio, Texas
Secretary Dr J W Jervey Jr, 101 Church St, Greenville, S C

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President Dr H L Brehmer, 221 W Central Ave, Albuquerque, N Mex
Secretary Dr A E Cruthirds, 1011 Professional Bldg, Phoenix, Ariz

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President Dr W M Dodge, 716 First National Bank Bldg, Battle Creek
Secretary-Treasurer Dr Kenneth Lowe, 25 W Michigan Ave, Battle Creek
Time Last Thursday of September, October, November, March, April and May

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Ray Parker, 218 Franklin St, Johnston, Pa
Secretary-Treasurer Dr J McClure Tyson, Deposit Nat'l Bank Bldg, DuBois

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President Dr Raymond C Cook, 701 Main St, Little Rock
Secretary Dr K W Cosgrove, Urquhart Bldg, Little Rock

COLORADO OPHTHALMOLOGICAL SOCIETY

President Dr C A Ringle, 912-9th Ave, Greeley
 Secretary Dr W A Ohmart, 1102 Republic Bldg, Denver
 Place University Club, Denver Time 7 30 p m, third Saturday of each month, October to May, inclusive

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR,
NOSE AND THROAT

President Dr F L Phillips, 405 Temple St, New Haven
 Secretary-Treasurer Dr W H Turnley, 1 Atlantic St, Stamford, Conn

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President Dr E N Maner, 247 Bull St, Savannah
 Secretary-Treasurer Dr C K McLaughlin, 567 Walnut St, Macon

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr F McK Ruby, Union City
 Secretary Dr Edwin W Dyar Jr, 23 E. Ohio St, Indianapolis
 Place French Lick Time First Wednesday in April

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr J K. Von Lackum, 117-3d St S E, Cedar Rapids
 Secretary-Treasurer Dr B M Merkel, 604 Locust St, Des Moines

LOUISIANA-MISSISSIPPI OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr Val H Fuchs, 200 Carondelet St, New Orleans
 Secretary-Treasurer Dr Edley H Jones, 1301 Washington St, Vicksburg, Miss

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY
AND OTOLARYNGOLOGY

Chairman Dr Robert H Fraser, 25 W Michigan Ave, Battle Creek
 Secretary Dr R G Laird, 114 Fulton St, Grand Rapids

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr George E McGeary, 920 Medical Arts Bldg, Minneapolis
 Secretary Dr William A Kennedy, 372 St Peter St, St Paul
 Time Second Friday of each month from October to May

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President Dr William Morrison, 208 N Broadway, Billings, Mont
 Secretary Dr Fritz D Hurd, 309 Medical Arts Bldg, Great Falls

NEBRASKA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha
 Secretary-Treasurer Dr John Peterson, 1307 N St, Lincoln

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY,
OTOLOGY AND RHINOLARYNGOLOGY

Chairman Dr B E Failing, 31 Lincoln Park, Newark
 Secretary Dr George Meyer, 410 Haddon Ave, Camden

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

Chairman Dr Searle B Marlow, 109 S Warren St, Syracuse
 Secretary Dr C Stewart Nash, 277 Alexander St, Rochester

NORTH CAROLINA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Hugh C Wolfe, 102 N Elm St, Greensboro
 Secretary Dr Vanderbilt F Couch, 105 W 4th St, Winston-Salem

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr T W Buckingham, 405 Broadway, Bismarck
Secretary-Treasurer. Dr F L Wicks, 516-6th St, Valley City

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Paul Neely, 1020 S W Taylor St, Portland
Secretary-Treasurer Dr Lewis Jordon, 1020 S W Taylor St, Portland
Place Good Samaritan Hospital, Portland Time Third Tuesday of each month

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

Acting President Dr N Darrell Harvey, 112 Waterman St, Providence
Secretary-Treasurer Dr Linley C Happ, 124 Waterman St, Providence
Place Rhode Island Medical Society Library, Providence Time 8 30 p m, second Thursday
in October, December, February and April

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr J L Sanders, 222 N Main St, Greenville
Secretary Dr J H Stokes, 125 W Cheves St, Florence

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Wesley Wilkerson, 700 Church St, Nashville
Secretary-Treasurer Dr W D Stinson, 124 Physicians and Surgeons Bldg, Memphis

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President Dr F H Rosebrough, 603 Navarro St, San Antonio
Secretary Dr M K McCullough, 1717 Pacific Ave, Dallas

UTAH OPHTHALMOLOGICAL SOCIETY

President Dr Everett B Muir, Boston Bldg, Salt Lake City
Secretary-Treasurer Dr Earl H Phillips, 623 Judge Bldg, Salt Lake City
Place University Club, Salt Lake City Time 7 00 p m, third Monday of each month

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President Dr Mortimer H Williams, 30½ Franklin Rd S W, Roanoke
Secretary-Treasurer Dr Meade Edmunds, 34 Franklin St, Petersburg

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE
AND THROAT SECTION

President Dr George Traugh, 309 Cleveland Ave, Fairmont
Secretary Dr Welch England, 621½ Market St, Parkersburg

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr E L Mather, 39 S Main St, Akron, Ohio
Secretary-Treasurer Dr V C Malloy, 2d National Bank Bldg, Akron, Ohio
Time First Monday in January, March, May and November

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President Dr B M Cline, 153 Peachtree St N E, Atlanta, Ga
Acting Secretary Dr A V Hallum 478 Peachtree St N E, Atlanta, Ga
Place Grady Hospital Time 6 00 p m, fourth Monday of each month, from October
to May

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman Dr Ernst Bodenheimer, 1212 Eutaw Pl, Baltimore
Secretary Dr Thomas R O'Rourke, 104 W Madison St., Baltimore
Place Medical and Chirurgical Faculty, 1211 Cathedral St Time 8 30 p m, fourth Thurs-
day of each month from October to March

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President Each member, in alphabetical order

Secretary Dr Luther E Wilson, 919 Woodward Bldg, Birmingham, Ala

Place Tutwiler Hotel Time 6 30 p m, second Tuesday of each month, September to May, inclusive

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President Dr William B Agan, 1 Nevins St, Brooklyn

Secretary-Treasurer Dr Benjamin C Rosenthal, 140 New York Ave, Brooklyn

Place Kings County Medical Society Bldg, 1313 Bedford Ave Time Third Thursday in February, April, May, October and December

BUFFALO OPHTHALMOLOGIC CLUB

President Dr Walter F King, 519 Delaware Ave, Buffalo

Secretary-Treasurer Dr Sheldon B Freeman, 196 Linwood Ave, Buffalo

Time Second Thursday of each month

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Each member, in alphabetical order

Secretary Dr Douglas Chamberlain, Chattanooga Bank Bldg, Chattanooga, Tenn

Place Mountain City Club Time Second Thursday of each month from September to May

CHICAGO OPHTHALMOLOGICAL SOCIETY

President Dr Vernon M Leech, 55 E Washington St, Chicago

Secretary Dr W A Mann, 30 N Michigan Ave, Chicago

Place Chicago Towers Club, 505 N Michigan Ave Time Third Monday of each month from October to May

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman Dr D T Vail, 441 Vine St, Cincinnati

Secretary Dr A A Levin, 441 Vine St, Cincinnati

Place Cincinnati General Hospital Time 7 45 p m, third Friday of each month except June, July and August

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman Dr Shandor Monson, 1621 Euclid Ave, Cleveland

Secretary Dr Carl Ellenberger, 14805 Detroit Ave, Cleveland

Time Second Tuesday in October, December, February and April

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman Dr Alfred Cowan, 1930 Chestnut St, Philadelphia

Clerk Dr W S Reese, 1901 Walnut St, Philadelphia

Time Third Thursday of every month from October to April, inclusive

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman Dr H D Emswiler, 370 E Town St, Columbus, Ohio

Secretary-Treasurer Dr D G Sanor, 206 E State St, Columbus, Ohio

Place The Neil House Time 6 p m, first Monday of each month

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Arthur Padillo, 414 Medical Professional Bldg, Corpus Christi, Texas

Secretary Dr Edgar G Mathis, 815 Medical Arts Bldg, Corpus Christi, Texas

Time Second Friday of each month from October to May

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr S F Harrington, 921 Medical Arts Bldg, Dallas, Texas

Secretary Dr Abell Hardin, Medical Arts Bldg, Dallas, Texas

Place Dallas Athletic Club Time 6 30 p m, first Tuesday of each month from October to June The November, January and March meetings are devoted to clinical work

DES MOINES ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr H C Schmitz, 604 Locust St, Des Moines, Iowa
 Secretary-Treasurer Dr Byron M Merkel, 604 Locust St, Des Moines, Iowa
 Time 7 45 p m, third Monday of every month from September to May

DETROIT OPHTHALMOLOGICAL CLUB

Chairman Dr Howell L Begle, 2730 E Jefferson Ave, Detroit
 Secretary Dr C W Lepard, 1025 David Whitney Bldg, Detroit
 Time 6 30 p m, first Wednesday of each month, November through April

DETROIT OPHTHALMOLOGICAL SOCIETY

President Dr Parker Heath, 1553 Woodward Ave, Detroit
 Secretary Dr Leland F Carter, 1553 Woodward Ave, Detroit
 Place Club rooms of Wayne County Medical Society Time Third Thursday of each month
 from November to April, inclusive

EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President Appointed at each meeting
 Secretary-Treasurer Dr Joseph L Holohan, 330 State St, Albany
 Time Third Wednesday in October, November, March, April, May and June

EASTERN PENNSYLVANIA ASSOCIATION OF EYE, EAR, NOSE AND THROAT PHYSICIANS

President Dr James E Landis, 232 N 6th St, Reading
 Secretary-Treasurer pro tem Dr Paul C Craig, 232 N 5th St, Reading
 Time Last week in April each year

FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Rex Howard, 602 W 10th St, Fort Worth, Texas
 Secretary-Treasurer Dr R H Gough, Medical Arts Bldg, Fort Worth, Texas
 Place Medical Hall, Medical Arts Bldg Time 7 30 p m, first Friday of each month except
 July and August

HOUSTON ACADEMY OF MEDICINE, OPHTHALMOLOGICAL AND
 OTO-LARYNGOLOGICAL SECTION

President Dr Felician J Slataper, 1110-1111 Medical Arts Bldg, Houston, Texas
 Secretary Dr Theo L Holland, 611 Medical Arts Bldg, Houston, Texas
 Place Medical Arts Bldg, Harris County Medical Society Rooms Time 8 p m, second
 Thursday of each month from September to June

INDIANAPOLIS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr Myron Harding, 23 E Ohio St, Indianapolis
 Secretary Dr Kenneth L Craft, 23 E Ohio St, Indianapolis
 Place Indianapolis Athletic Club Time 6 30 p m, second Thursday of each month from
 November to May

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President Dr Edgar Johnson, 906 Grand Ave, Kansas City, Mo
 Secretary Dr W E Keith, 1103 Grand Ave, Kansas City, Mo
 Time Third Thursday of each month from October to June The November, January and
 March meetings are devoted to clinical work

LONG BEACH EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Dr Harold Snow, 614 S Pacific Ave, San Pedro, Calif
 Secretary-Treasurer Dr Oliver R Nees, 508 Times Bldg, Long Beach, Calif
 Place Professional Bldg Time Last Wednesday of each month from October to May

LOS ANGELES SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr Sylvester H Welch, 102 N Brand Blvd, Glendale, Calif
 Secretary-Treasurer Dr Orrie E Ghrist, 210 N Central Ave, Glendale, Calif
 Place Los Angeles County Medical Association Bldg, 1925 Wilshire Blvd Time 6 00 p m,
 fourth Monday of each month from September to May, inclusive

LOUISVILLE EYE AND EAR SOCIETY

President Dr Joseph S Heitger, Heyburn Bldg, Louisville, Ky
 Secretary-Treasurer Dr J W Fish, 321 W Broadway, Louisville, Ky
 Place Brown Hotel Time 6 30 p m, second Thursday of each month from September to May, inclusive

LOWER ANTHRACITE EYE, EAR, NOSE AND THROAT SOCIETY

Chairman Each member in alphabetical order
 Secretary Dr James J Monohan, 31 S Jardin St, Shenandoah, Pa

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF
OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr P S Constantinople, 1835 I St N W, Washington
 Secretary Dr Frazier Williams, 1801 I St N W, Washington
 Place 1718 M St N W Time 8 p m, third Friday of each month from October to April, inclusive

MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Each member in alphabetical order
 Secretary Dr Sam H Sanders, 1089 Madison Ave, Memphis, Tenn
 Place Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital Time 8 p m, second Tuesday of each month from September to May

MILWAUKEE OTO-OPHTHALMIC SOCIETY

President Dr Edwin C Bach, 324 E Wisconsin Ave, Milwaukee
 Secretary-Treasurer Dr Ralph T Rank, 238 W Wisconsin Ave, Milwaukee
 Place University Club Time 6 30 p m, second Tuesday of each month

MONTGOMERY COUNTY MEDICAL SOCIETY

Chairman Dr H V Dutrow, 1040 Fidelity Medical Bldg, Dayton, Ohio
 Secretary-Treasurer Dr Maitland D Place, 981 Reibold Bldg, Dayton, Ohio
 Place Van Cleve Hotel Time 6 30 p m, first Tuesday of each month from October to June, inclusive

MONTREAL OPHTHALMOLOGICAL SOCIETY

President Dr J Rosenbaum, 1396 Ste Catherine St W, Montreal, Canada
 Secretary Dr L Tessier, 1230 St Joseph Blvd E, Montreal, Canada
 Time Second Thursday of October, December, February and April

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman Dr M M Cullom, 700 Church St, Nashville, Tenn
 Secretary Dr R E Sullivan, 432 Doctors Bldg, Nashville, Tenn
 Place St Thomas Hospital Time 8 p m, third Monday of each month from October to May

NEW HAVEN OPHTHALMOLOGICAL SOCIETY

President Dr William H Ryder, 185 Church St, New Haven, Conn
 Secretary Dr Frederick A Wiess, 255 Bradley St, New Haven, Conn

NEW ORLEANS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President Dr W B Clark, 1012 American Bank Bldg, New Orleans
 Secretary Dr Mercer G Lynch, 1018 Maison Blanche Bldg, New Orleans
 Place Louisiana State University Medical Bldg Time 8 p m, second Tuesday of each month from October to May

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman Dr Frank C Keil, 660 Madison Ave, New York
 Secretary Dr Willis S Knighton, 121 E 61st St, New York
 Time 8 30 p m, third Monday of every month from October to May, inclusive

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

President Dr Sigmund Agatston, 875-5th Ave, New York
 Secretary Dr Benjamin Esterman, 983 Park Ave, New York
 Place Squibb Hall, 745-5th Ave Time 8 p m, First Monday of each month from October to May, inclusive

OKLAHOMA CITY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President Dr James P Luton, 117 N Broadway, Oklahoma City
 Secretary Dr Harvey O Randel, 117 N Broadway, Oklahoma City
 Place University Hospital Time Second Tuesday of each month from September to May

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND
 OTO-LARYNGOLOGICAL SOCIETY

President Dr D D Stonecypher, Nebraska City, Neb
 Secretary-Treasurer Dr W Howard Morrison, 1500 Medical Arts Bldg, Omaha
 Place Omaha Club, 20th and Douglas Sts, Omaha Time 6 p m dinner, 7 p m program,
 third Wednesday of each month from October to May

PASSAIC-BERGEN OPHTHALMOLOGICAL CLUB

President Dr Thomas Sanfacon, 340 Park Ave, Paterson, N J
 Secretary-Treasurer Dr J Averbach, 435 Clinton Ave, Clinton, N J
 Place Paterson Eye and Ear Infirmary Time 9 p m, last Friday of every month except
 June, July and August

PHILADELPHIA COUNTY MEDICAL SOCIETY, EYE SECTION

President Dr Wilfred E Fry, 1819 Chestnut St, Philadelphia
 Secretary Dr Glen Gregory Gibson, 255 S 17th St, Philadelphia
 Time First Thursday of each month from October to May

PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President Dr John B McMurray, 6 S Main St, Washington, Pa
 Secretary Dr George H Shuman, 351-5th Ave, Pittsburgh
 Place Pittsburgh Academy of Medicine Bldg Time Fourth Monday of each month, except
 June, July, August and September

READING EYE, EAR, NOSE AND THROAT SOCIETY

President Dr R M Brickbauer, Shillington, Pa
 Secretary Dr Paul C Craig, 232 N 5th St, Reading, Pa
 Place Wyomissing Club Time 6 30 p m, third Wednesday of each month from October
 to July

RICHMOND OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President Dr Peter N Pastore, Medical College of Virginia, Richmond, Va
 Secretary Dr Clifford A Folkes, Professional Bldg, Richmond, Va
 Place Westmoreland Club Time 6 p m, second Monday of each month from October
 to May

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

President Dr Frank Barber, 75 S Fitzhugh St, Rochester, N Y
 Secretary-Treasurer Dr Charles T Sullivan, 277 Alexander St, Rochester, N Y

ST LOUIS OPHTHALMIC SOCIETY

President Dr C C Beisbarth, 3720 Washington Blvd, St Louis
 Secretary Dr H R Hildreth, 508 N Grand Blvd, St Louis
 Place Oscar Johnson Institute Time Clinical meeting, 5 30 p m, dinner and scientific
 meeting 6 30 p m, fourth Friday of each month from October to April, inclusive, except
 December

SAN ANTONIO OPHTHALMO-OTO-LARYNGOLOGICAL SOCIETY

President Dr Dan Russell, 705 E Houston St, San Antonio, Texas
 Secretary-Treasurer Dr P G Bowen, 315 Camden St, San Antonio, Texas
 Place Bexar County Medical Library Time 8 p m, first Tuesday of each month from
 October to May

SAN FRANCISCO COUNTY MEDICAL SOCIETY, SECTION ON EYE,
 EAR, NOSE AND THROAT

Chairman Dr Roy H Parkinson, 870 Market St, San Francisco
 Secretary Dr A G Rawlins, 384 Post St, San Francisco
 Place Society's Bldg, 2180 Washington St, San Francisco Time Fourth Tuesday of every
 month except June, July and December

SHREVEPORT EYE, EAR, NOSE AND THROAT SOCIETY

President Dr David C Swearingen, Slattery Bldg, Shreveport, La
 Secretary-Treasurer Dr Kenneth Jones, Medical Arts Bldg, Shreveport, La
 Place Shreveport Charity Hospital Time 7 30 p m, first Monday of every month except
 July, August and September

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